```
=> d his

     (FILE 'CAPLUS' ENTERED AT 14:08:59 ON 22 DEC 2003)
               DEL HIS Y

     FILE 'REGISTRY' ENTERED AT 14:10:43 ON 22 DEC 2003
               ACT MOHAMED/A
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L1              STR
L2              SCR 1199
L3           46 SEA FILE=REGISTRY SSS FUL L1 AND L2
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L4            8 S L3 AND F=2 AND CL=2
L5           38 S L3 NOT L4

     FILE 'HCAPLUS' ENTERED AT 14:11:20 ON 22 DEC 2003
L6           9 S L4
L7           12 S L5
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FILE 'REGISTRY' ENTERED AT 14:13:02 ON 22 DEC 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   21 DEC 2003  HIGHEST RN 629597-20-2
DICTIONARY FILE UPDATES:  21 DEC 2003  HIGHEST RN 629597-20-2

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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L1                STR
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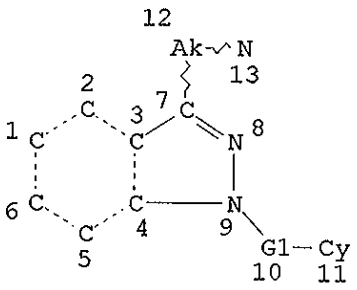


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CONNECT IS E2  RC AT  12
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS M1-X2 C  AT  12

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS  13

STEREO ATTRIBUTES: NONE
L2              SCR 1199
L3           46 SEA FILE=REGISTRY SSS FUL L1 AND L2

100.0% PROCESSED  15268 ITERATIONS                    46 ANSWERS
SEARCH TIME: 00.00.01
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L4            8 S L3 AND F=2 AND CL=2
L5           38 S L3 NOT L4


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FILE 'HCAPLUS' ENTERED AT 14:13:17 ON 22 DEC 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 22 Dec 2003  VOL 139 ISS 26
FILE LAST UPDATED: 21 Dec 2003  (20031221/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> d que nos l6
L1              STR
L2              SCR 1199
L3           46 SEA FILE=REGISTRY SSS FUL L1 AND L2
L4            8 SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 AND F=2 AND CL=2
L6            9 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L4


=> d que nos l7
L1              STR
L2              SCR 1199
L3           46 SEA FILE=REGISTRY SSS FUL L1 AND L2
L4            8 SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 AND F=2 AND CL=2
L5           38 SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 NOT L4
L7           12 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L5


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L6   ANSWER 1 OF 9  HCAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2003:262705  HCAPLUS
DOCUMENT NUMBER:          139:127220
TITLE:                    Discovery of potent peptide-mimetic antagonists for
```

the human thrombin receptor, protease-activated receptor-1 (PAR-1)

AUTHOR(S): Maryanoff, Bruce E.; Zhang, Han-Cheng; Andrade-Gordon, Patricia; Derian, Claudia K.

CORPORATE SOURCE: Drug Discovery, Johnson and Johnson Pharmaceutical Research and Development, Spring House, PA, 19477-0776, USA

SOURCE: Current Medicinal Chemistry: Cardiovascular & Hematological Agents (2003), 1(1), 13-36
CODEN: CMCCDP; ISSN: 1568-0169

PUBLISHER: Bentham Science Publishers Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Protease-activated receptors (PARs) represent a unique family of seven-transmembrane G-protein-coupled receptors, which are enzymically cleaved to expose a new extracellular N-terminus that acts as a tethered activating ligand. PAR-1 is cleaved and activated by the serine protease α-thrombin, is expressed in various tissues (e.g., platelets and vascular cells), and is involved in cellular responses associated with hemostasis, proliferation, and tissue injury. By using a de novo design approach, we have discovered a series of potent heterocycle-based peptide-mimetic antagonists of PAR-1, exemplified by advanced leads RWJ-56110 and RWJ-58259. These compds. are potent, selective PAR-1 antagonists, devoid of PAR-1 agonist and thrombin inhibitory activity: they bind to PAR-1, interfere with calcium mobilization and cellular functions associated with PAR-1, and do not affect PAR-2, PAR-3, or PAR-4. RWJ-56110 was determined to be a direct inhibitor of PAR-1 activation and internalization, without affecting PAR-1 N-terminal cleavage. At high concns. of α-thrombin, RWJ-56110 fully blocked activation responses in human vascular cells, but not in human platelets; whereas, at high concns. of TRAP-6, RWJ-56110 blocked activation responses in both cell types. This result is consistent with the presence of another thrombin receptor on human platelets, namely PAR-4. RWJ-56110 and RWJ-58259 clearly interrupt the binding of a tethered ligand to its receptor. RWJ-58259 demonstrated antirestenotic activity in a rat balloon angioplasty model and antithrombotic activity in a cynomolgus monkey arterial injury model. Such PAR-1 antagonists should not only serve as useful tools to delineate the physiol. and pathophysiol. roles of PAR-1, but also may have therapeutic potential for treating thrombosis and restenosis in humans.

CC 1-0 (Pharmacology)
Section cross-reference(s): 27, 28, 34

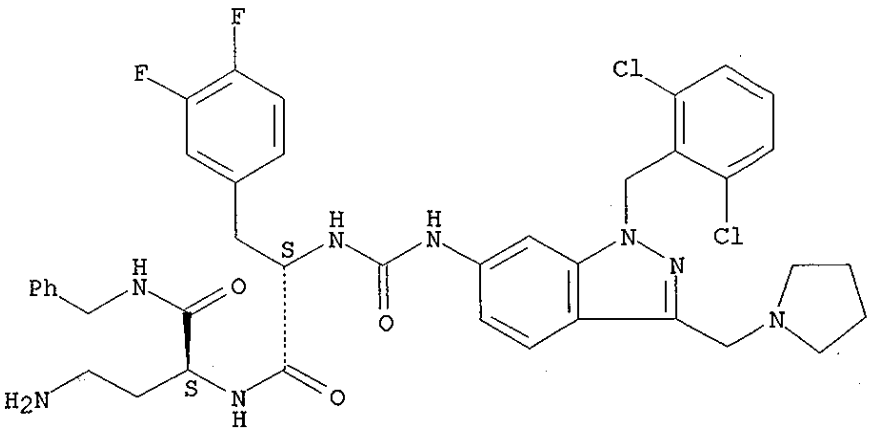
IT 252889-88-6, RWJ-56110 **315203-31-7**, RWJ-58259
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(discovery of potent peptide-mimetic antagonists for human thrombin receptor, protease-activated receptor-1 (PAR-1))

IT **315203-31-7**, RWJ-58259
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(discovery of potent peptide-mimetic antagonists for human thrombin receptor, protease-activated receptor-1 (PAR-1))

RN 315203-31-7 HCAPLUS

CN Benzenepropanamide, N-[(1S)-3-amino-1-[[(phenylmethyl)amino]carbonyl]propyl]-α-[[[[1-[(2,6-dichlorophenyl)methyl]-3-(1-pyrrolidinylmethyl)-1H-indazol-6-yl]amino]carbonyl]amino]-3,4-difluoro-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

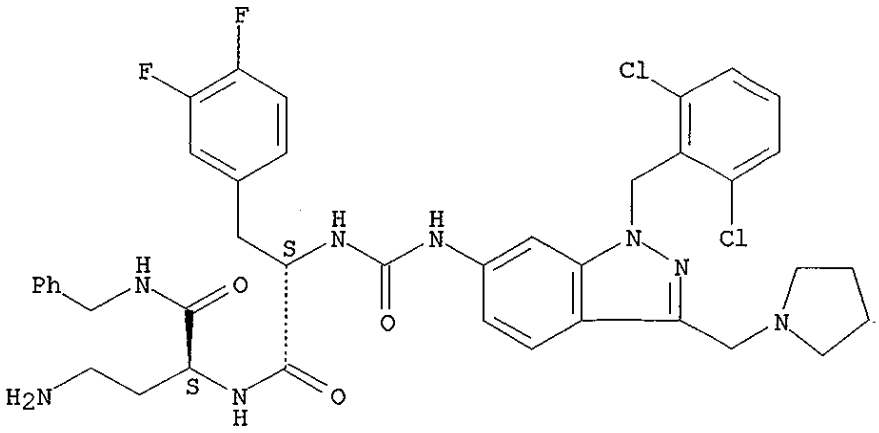


REFERENCE COUNT: 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:262511 HCAPLUS
TITLE: Blockade of the thrombin receptor protease-activated receptor-1 with a small-molecule antagonist prevents thrombus formation and vascular occlusion in nonhuman primates. [Erratum to document cited in CA139:30490]
AUTHOR(S): Derian, Claudia K.; Damiano, Bruce P.; Addo, Michael F.; Darrow, Andrew L.; D'Andrea, Michael R.; Nedelman, Mark; Zhang, Han-Cheng; Maryanoff, Bruce E.; Andrade-Gordon, Patricia
CORPORATE SOURCE: Johnson and Johnson Pharmaceutical Research and Development, Spring House, PA, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2003), 305(1), 402
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal; Errata
LANGUAGE: English
AB An erratum.
CC 1-8 (Pharmacology)
IT INDEXING IN PROGRESS
IT **315203-31-7**, RWJ-58259
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(blockade of thrombin receptor protease-activated receptor-1 with small-mol. antagonist prevents thrombus formation and vascular occlusion in nonhuman primates (Erratum))
IT **315203-31-7**, RWJ-58259
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(blockade of thrombin receptor protease-activated receptor-1 with small-mol. antagonist prevents thrombus formation and vascular occlusion in nonhuman primates (Erratum))
RN 315203-31-7 HCAPLUS
CN Benzenepropanamide, N-[(1S)-3-amino-1-[[(phenylmethyl)amino]carbonyl]propy

l]-α-[[[[1-[(2,6-dichlorophenyl)methyl]-3-(1-pyrrolidinylmethyl)-1H-indazol-6-yl]amino]carbonyl]amino]-3,4-difluoro-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2003:98469 HCAPLUS
DOCUMENT NUMBER: 139:30490
TITLE: Blockade of the thrombin receptor protease-activated receptor-1 with a small-molecule antagonist prevents thrombus formation and vascular occlusion in nonhuman primates
AUTHOR(S): Derian, Claudia K.; Damiano, Bruce P.; Addo, Michael F.; Darrow, Andrew L.; D'andrea, Michael R.; Nedelman, Mark; Zhang, Han-Cheng; Maryanoff, Bruce E.; Andrade-Gordon, Patricia
CORPORATE SOURCE: Johnson and Johnson Pharmaceutical Research and Development, Spring House, PA, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2003), 304(2), 855-861
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Although it is well recognized that human platelet responses to α-thrombin are mediated by the protease-activated receptors PAR-1 and PAR-4, their role and relative importance in platelet-dependent human disease has not yet been elucidated. Because the expression profile of PARs in platelets from nonprimates differs from humans, we used cynomolgus monkeys to evaluate the role of PAR-1 in thrombosis. Based on reverse transcription-polymerase chain reaction, PAR expression in platelets from cynomolgus monkeys consisted primarily of PAR-1 and PAR-4, thereby mirroring the profile of human platelets. We probed the role of PAR-1 in a primate model of vascular injury-induced thrombosis with the selective PAR-1 antagonist (αS)-N-[(1S)-3-amino-1-[[(phenylmethyl)amino]carbonyl]propyl]-α-[[[[1-(2,6-dichlorophenyl)methyl]-3-(1-pyrrolidinylmethyl)-1H-indazol-6-yl]amino]carbonyl]amino]-3,4-difluorobenzenepropanamide (RWJ-58259).

After pretreatment with RWJ-58259 or vehicle, both carotid arteries of anesthetized monkeys were electrolytically injured and blood flow was monitored for 60 min. Time to occlusion was significantly extended after RWJ-58259 administration (27±3 to 53±8 min; $p < 0.048$). Vessels from three of the five treated animals remained patent. Ex vivo platelet aggregation measurements indicated complete PAR-1 inhibition, as well as an operational PAR-4 response. Immunohistochem. staining of mural thrombi with antibodies to the platelet marker CD61 and fibrinogen indicated that RWJ-58259 significantly reduced thrombus platelet deposition. Drug treatment had no effect on key hematol. or coagulation parameters. Our results provide direct evidence that PAR-1 is the primary receptor that mediates α-thrombin's prothrombotic actions in primates and suggest that PAR-1 antagonists may have potential for the treatment of thrombotic disorders in humans.

CC 1-8 (Pharmacology)

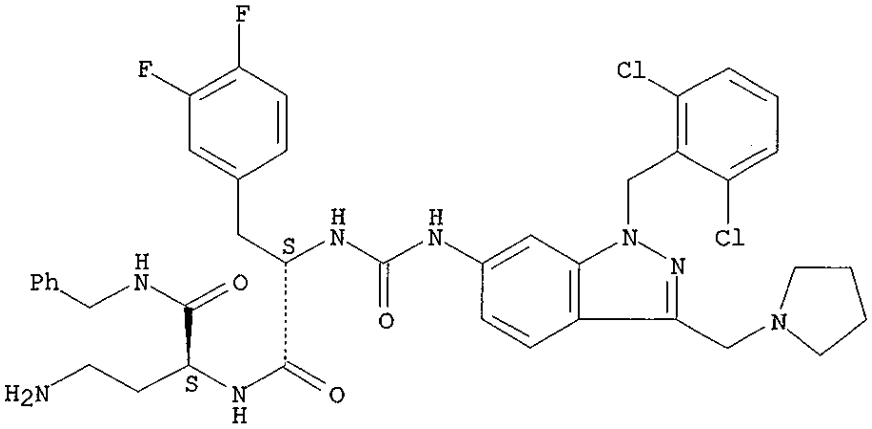
IT **315203-31-7,** RWJ-58259
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(blockade of thrombin receptor protease-activated receptor-1 with small-mol. antagonist prevents thrombus formation and vascular occlusion in nonhuman primates)

IT **315203-31-7,** RWJ-58259
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(blockade of thrombin receptor protease-activated receptor-1 with small-mol. antagonist prevents thrombus formation and vascular occlusion in nonhuman primates)

RN 315203-31-7 HCAPLUS

CN Benzenepropanamide, N-[(1S)-3-amino-1-[[(phenylmethyl)amino]carbonyl]propyl]-α-[[[[1-[(2,6-dichlorophenyl)methyl]-3-(1-pyrrolidinylmethyl)-1H-indazol-6-yl]amino]carbonyl]amino]-3,4-difluoro-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:294231 HCAPLUS
DOCUMENT NUMBER: 136:304058

TITLE: Method for reducing or preventing the establishment, growth or metastasis of cancer by administering PAR-1 and optionally PAR-2 antagonists
INVENTOR(S): D'andrea, Michael; Derian, Claudia; Woodrow, Hal Brent
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 38 pp., Cont.-in-part of U.S. Ser. No. 603,229.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

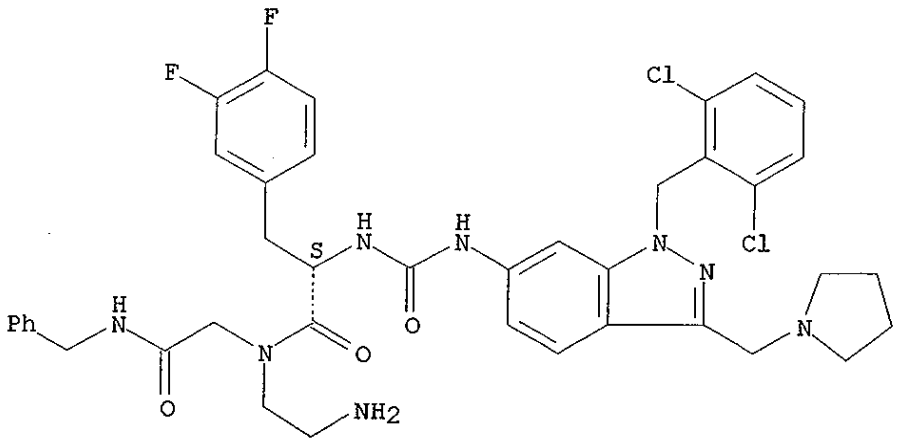
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002045581	A1	20020418	US 2001-865869	20010525
US 6365617	B1	20020402	US 2000-603229	20000626

PRIORITY APPLN. INFO.: US 1999-141555P P 19990629
US 2000-603229 A2 20000626
OTHER SOURCE(S): MARPAT 136:304058

AB We have discovered a method of modifying the tumor cell microenvironment to reduce or prevent the establishment, growth or metastasis of malignant cells comprising administering to a patient having malignant cells a pharmaceutically effective amount of a PAR-1 inhibitor and optionally a PAR-2 inhibitor to prevent or reduce activation of normal cells within the tumor microenvironment. This method also has the effect in some patients of modulating the immune system to facilitate a more efficient immune response to malignant cells and maybe coupled with cytokine therapy and T-cell therapy to enhance the patient's immune response to the malignant cells.

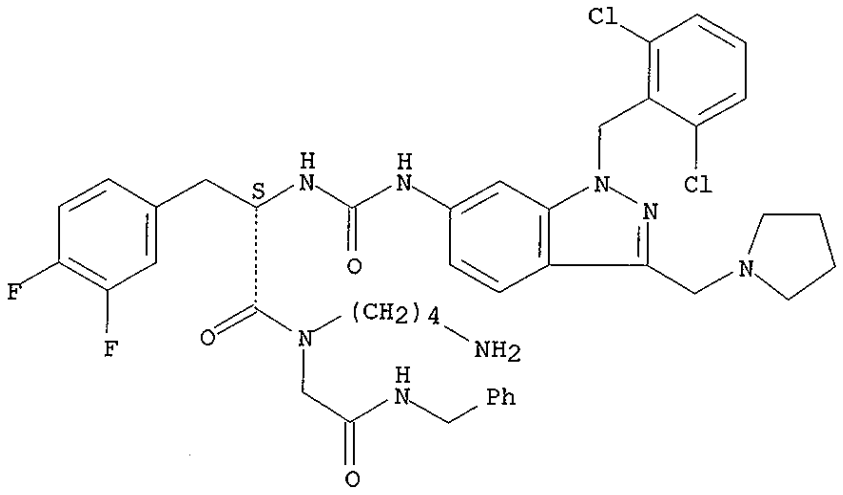
IC ICM A61K038-05
ICS C07D275-04; C07D261-20; C07D231-56
NCL 514019000
CC 1-6 (Pharmacology)
Section cross-reference(s): 15
IT 81627-83-0, M-CSF 143011-72-7, Granulocyte colony-stimulating factor **314751-99-0** 314752-00-6 **314752-01-7** 314752-02-8 314752-03-9 314752-04-0 314752-05-1 314752-06-2 **314752-07-3** 314752-08-4 314752-09-5 314752-10-8 314752-11-9 314752-12-0 314752-13-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for reducing or preventing the establishment, growth or metastasis of cancer by administering PAR-1 and optionally PAR-2 antagonists)
IT **314751-99-0 314752-01-7 314752-07-3**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for reducing or preventing the establishment, growth or metastasis of cancer by administering PAR-1 and optionally PAR-2 antagonists)
RN 314751-99-0 HCAPLUS
CN Glycinamide, N-[[[1-[(2,6-dichlorophenyl)methyl]-3-(1-pyrrolidinylmethyl)-1H-indazol-6-yl]amino]carbonyl]-3,4-difluoro-L-phenylalanyl-N2-(2-aminoethyl)-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



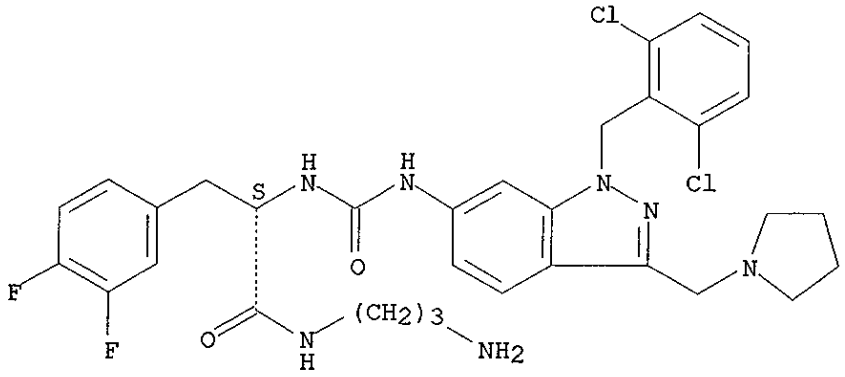
RN 314752-01-7 HCAPLUS
CN Glycinamide, N-[[[1-[(2,6-dichlorophenyl)methyl]-3-(1-pyrrolidinylmethyl)-1H-indazol-6-yl]amino]carbonyl]-3,4-difluoro-L-phenylalanyl-N2-(4-aminobutyl)-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 314752-07-3 HCAPLUS
CN Benzenepropanamide, N-(3-aminopropyl)-α-[[[[1-[(2,6-dichlorophenyl)methyl]-3-(1-pyrrolidinylmethyl)-1H-indazol-6-yl]amino]carbonyl]amino]-3,4-difluoro-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:241341 HCAPLUS
DOCUMENT NUMBER: 136:257235
TITLE: Indazole peptidomimetic PAR-1 antagonists and PAR-2 antagonists as potential agents for controlling cancer metastasis
INVENTOR(S): D'Andrea, Michael; Derian, Claudia; Woodrow, Hal Brent
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 44 pp., Cont.-in-part of U.S. Ser. No. 603,338.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002037860	A1	20020328	US 2001-865511	20010525
US 2003199455	A1	20031023	US 2003-403218	20030331

PRIORITY APPLN. INFO.: US 1999-141553P P 19990629
US 2000-603338 A2 20000626
OTHER SOURCE(S): MARPAT 136:257235

AB We have discovered a method of modifying the tumor cell microenvironment to reduce or prevent the establishment, growth or metastasis of malignant cells comprising administering to a patient having malignant cells a pharmaceutically effective amount of an indazole peptidomimetic PAR-1 inhibitor and optionally a PAR-2 inhibitor to prevent or reduce activation of normal cells within the tumor microenvironment. This method also has the effect in some patients of modulating the immune system to facilitate a more efficient immune response to malignant cells and maybe coupled with cytokine therapy and T-cell therapy to enhance the patient's immune response to the malignant cells.

IC ICM A61K038-05
ICS C07D231-56
NCL 514019000
CC 1-6 (Pharmacology)
Section cross-reference(s): 28
IT 107-15-3, 1,2-Ethanediamine, reactions 123-75-1, Pyrrolidine, reactions 4769-96-4, 6-Nitroindole 125238-99-5 **315203-33-9D**, resin-bound 315203-45-3D, resin-bound 405271-58-1D, resin-bound

RL: RCT (Reactant); RACT (Reactant or reagent)
(indazole peptidomimetic PAR-1 antagonists and PAR-2 antagonists as potential agents for controlling cancer metastasis)

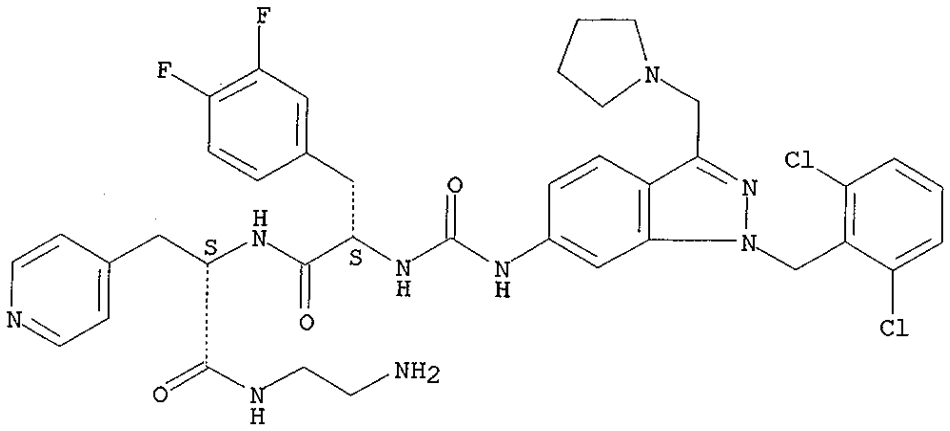
IT **315203-31-7P** 315203-32-8P **315203-33-9P**
315203-34-0P 315203-35-1P 315203-36-2P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(indazole peptidomimetic PAR-1 antagonists and PAR-2 antagonists as potential agents for controlling cancer metastasis)

IT **315203-33-9D**, resin-bound
RL: RCT (Reactant); RACT (Reactant or reagent)
(indazole peptidomimetic PAR-1 antagonists and PAR-2 antagonists as potential agents for controlling cancer metastasis)

RN 315203-33-9 HCAPLUS

CN L-Alaninamide, N-[[[1-[(2,6-dichlorophenyl)methyl]-3-(1-pyrrolidinylmethyl)-1H-indazol-6-yl]amino]carbonyl]-3,4-difluoro-L-phenylalanyl-N-(2-aminoethyl)-3-(4-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

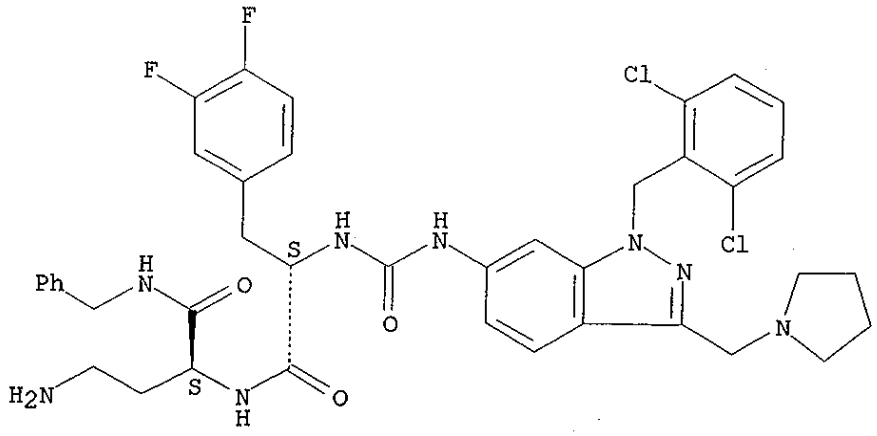


IT **315203-31-7P 315203-33-9P 315203-34-0P**
315203-35-1P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(indazole peptidomimetic PAR-1 antagonists and PAR-2 antagonists as potential agents for controlling cancer metastasis)

RN 315203-31-7 HCAPLUS

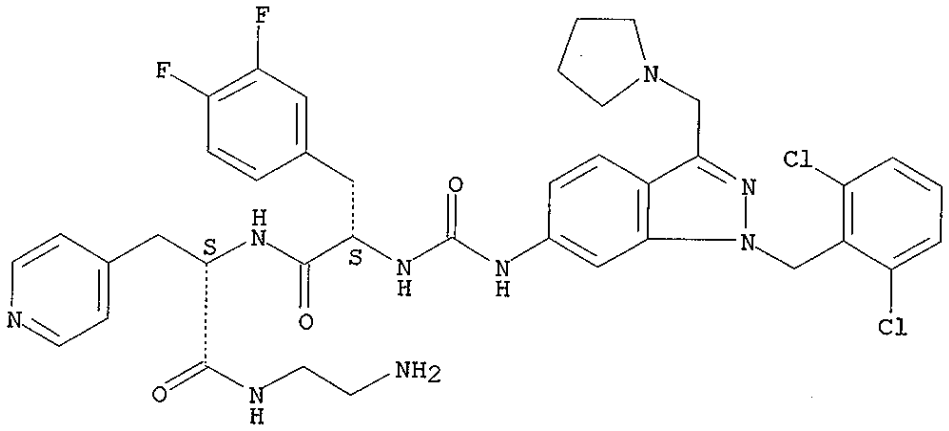
CN Benzenepropanamide, N-[(1S)-3-amino-1-[[(phenylmethyl)amino]carbonyl]propyl]-α-[[[[1-[(2,6-dichlorophenyl)methyl]-3-(1-pyrrolidinylmethyl)-1H-indazol-6-yl]amino]carbonyl]amino]-3,4-difluoro-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



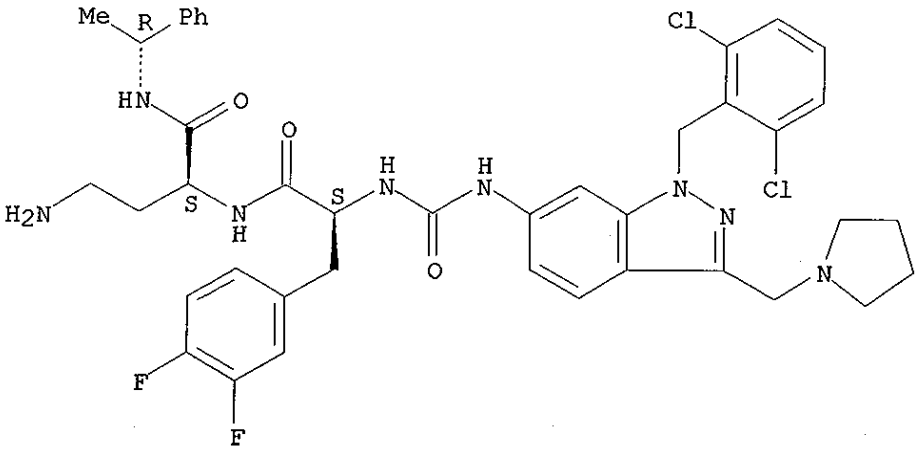
RN 315203-33-9 HCAPLUS
CN L-Alaninamide, N-[[[1-[(2,6-dichlorophenyl)methyl]-3-(1-pyrrolidinylmethyl)-1H-indazol-6-yl]amino]carbonyl]-3,4-difluoro-L-phenylalanyl-N-(2-aminoethyl)-3-(4-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



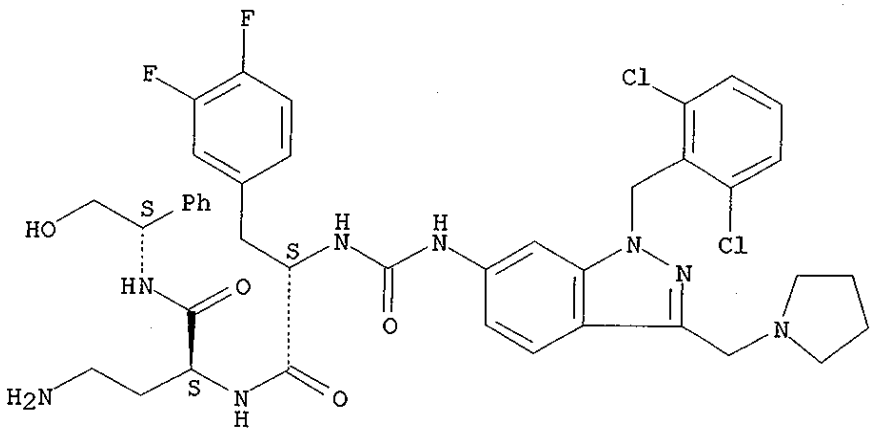
RN 315203-34-0 HCAPLUS
CN Benzenepropanamide, N-[(1S)-3-amino-1-[[[(1R)-1-phenylethyl]amino]carbonyl]propyl]-α-[[[[1-[(2,6-dichlorophenyl)methyl]-3-(1-pyrrolidinylmethyl)-1H-indazol-6-yl]amino]carbonyl]amino]-3,4-difluoro-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 315203-35-1 HCAPLUS
CN Benzenepropanamide, N-[(1S)-3-amino-1-[[[(1S)-2-hydroxy-1-phenylethyl]amino]carbonyl]propyl]-α-[[[[1-[(2,6-dichlorophenyl)methyl]-3-(1-pyrrolidinylmethyl)-1H-indazol-6-yl]amino]carbonyl]amino]-3,4-difluoro-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:454255 HCAPLUS
DOCUMENT NUMBER: 135:266910
TITLE: Administration of a potent antagonist of protease-activated receptor-1 (PAR-1) attenuates vascular restenosis following balloon angioplasty in rats
AUTHOR(S): Andrade-Gordon, Patricia; Derian, Claudia K.; Maryanoff, Bruce E.; Zhang, Han-Cheng; Addo, Michael F.; Cheung, Wai-Man; Damiano, Bruce P.; D'Andrea, Michael R.; Darrow, Andrew L.; De Garavilla, Lawrence; Eckardt, Annette J.; Giardino, Edward C.; Haertlein, Barbara J.; McComsey, David F.

CORPORATE SOURCE: Drug Discovery, The R. W. Johnson Pharmaceutical Research Institute, Spring House, PA, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2001), 298(1), 34-42
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Human platelets possess two distinct thrombin-activated receptors, PAR-1 (protease-activated receptor-1) and PAR-4, whereas human vascular smooth muscle cells possess only PAR-1. Although such thrombin receptors have been studied extensively in vitro, their physiol. roles are still rather ill-defined. The authors have now employed a potent, selective PAR-1 antagonist, RWJ-58259, to probe the in vivo significance of PAR-1 in thrombosis and vascular injury. RWJ-58259 was examined in two thrombosis models in guinea pigs: the arteriovenous (A-V) shunt assay (monitoring thrombus weight) and the Rose Bengal intravascular photoactivation assay (monitoring time to occlusion). Administration of RWJ-58259 (10 mg/kg, total i.v. dose) did not inhibit thrombus formation in either thrombosis model, although local, intrashunt delivery in the A-V shunt model did elicit a modest antithrombotic effect (thrombus weight reduction from 35 to 24 mg). These results are consistent with the presence of more than one thrombin-sensitive receptor on guinea pig platelets, in analogy with human platelets. Indeed, the authors were able to establish that guinea pig platelets express three thrombin receptors, PAR-1, PAR-3, and PAR-4. The authors also examined RWJ-58259 in a vascular restenosis model involving balloon angioplasty in rats. Perivascular administration of RWJ-58259 (10 mg) significantly reduced neointimal thickness (77 μm to 45 μm), clearly demonstrating an important role for PAR-1 in vascular injury. From these results, it is evident that a PAR-1 antagonist is not especially effective for treating platelet-dependent thrombosis; however, it could well be beneficial for treating restenosis attendant to arterial injury.

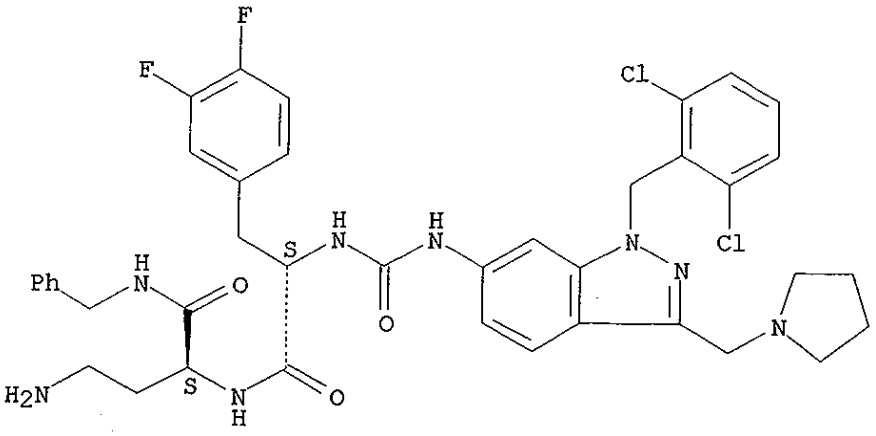
CC 1-8 (Pharmacology)
Section cross-reference(s): 14

IT **315203-31-7**, RWJ-58259
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(administration of a potent antagonist of protease-activated receptor-1 (PAR-1) attenuates vascular restenosis following balloon angioplasty in rats in relation to thrombosis and antithrombotic effect)

IT **315203-31-7**, RWJ-58259
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(administration of a potent antagonist of protease-activated receptor-1 (PAR-1) attenuates vascular restenosis following balloon angioplasty in rats in relation to thrombosis and antithrombotic effect)

RN 315203-31-7 HCAPLUS
CN Benzenepropanamide, N-[(1S)-3-amino-1-[[(phenylmethyl)amino]carbonyl]propyl]-α-[[[[1-[(2,6-dichlorophenyl)methyl]-3-(1-pyrrolidinylmethyl)-1H-indazol-6-yl]amino]carbonyl]amino]-3,4-difluoro-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:192750 HCAPLUS
DOCUMENT NUMBER: 134:335986
TITLE: Discovery and Optimization of a Novel Series of Thrombin Receptor (PAR-1) Antagonists: Potent, Selective Peptide Mimetics Based on Indole and Indazole Templates
AUTHOR(S): Zhang, Han-Cheng; Derian, Claudia K.; Andrade-Gordon, Patricia; Hoekstra, William J.; McComsey, David F.; White, Kimberly B.; Poulter, Brenda L.; Addo, Michael F.; Cheung, Wai-Man; Damiano, Bruce P.; Oksenberg, Donna; Reynolds, Elwood E.; Pandey, Anjali; Scarborough, Robert M.; Maryanoff, Bruce E.
CORPORATE SOURCE: Drug Discovery, The R. W. Johnson Pharmaceutical Research Institute, Spring House, PA, 19477, USA
SOURCE: Journal of Medicinal Chemistry (2001), 44(7), 1021-1024
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Coughlin and coworkers identified the first example of a thrombin receptor (protease-activated receptor-1, PAR-1), a member of the vast superfamily of seven-transmembrane, G-protein-coupled receptors. PAR-1 mediates most of the cellular actions of thrombin, such as platelet aggregation, cell proliferation, inflammatory responses, and neurodegeneration. Thus, this receptor is an attractive drug discovery target for the possible treatment of various disorders such as thrombosis, restenosis, atherosclerosis, inflammation, cancer metastasis, and stroke. Here we describe a second-generation indazole-based SFLLR peptide mimetics, an archetype of which is RWJ-58259 a potent, selective PAR-1 antagonist with an improved in vivo cardiovascular safety profile, demonstrated in vivo antirestenotic activity in a rat balloon angioplasty model.

CC 1-3 (Pharmacology)
Section cross-reference(s): 28

IT **315203-31-7P**, RWJ 58259
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or

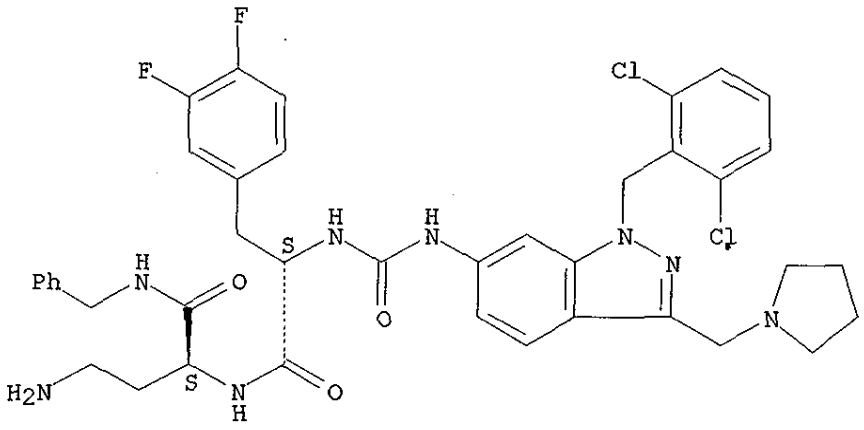
effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of a novel series of peptide mimetics based on indole and indazole templates as thrombin receptor (PAR-1) antagonists)

IT **315203-31-7P**, RWJ 58259
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of a novel series of peptide mimetics based on indole and indazole templates as thrombin receptor (PAR-1) antagonists)

RN 315203-31-7 HCAPLUS

CN Benzenepropanamide, N-[(1S)-3-amino-1-[[(phenylmethyl)amino]carbonyl]propyl]-α-[[[[1-[(2,6-dichlorophenyl)methyl]-3-(1-pyrrolidinylmethyl)-1H-indazol-6-yl]amino]carbonyl]amino]-3,4-difluoro-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:12481 HCAPLUS
DOCUMENT NUMBER: 134:71905
TITLE: Preparation of indazole peptidomimetics as thrombin receptor antagonists
INVENTOR(S): Zhang, Han-cheng; Maryanoff, Bruce E.; Pandey, Anjali; Scarborough, Robert M.
PATENT ASSIGNEE(S): Ortho-Mcneil Pharmaceutical, Inc., USA; Cor Therapeutics, Inc.
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

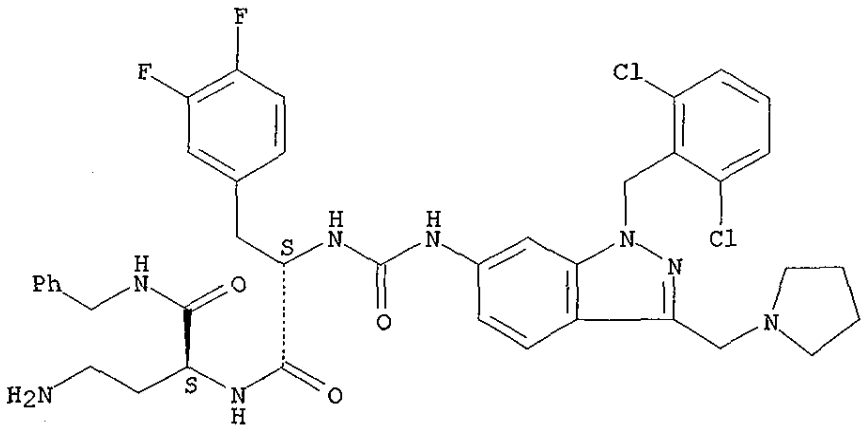
WO 2001000656 A2 20010104 WO 2000-US17718 20000628
WO 2001000656 A3 20010525
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
US 2003199455 A1 20031023 US 2003-403218 20030331
PRIORITY APPLN. INFO.: US 1999-141553P P 19990629
US 2000-603338 A 20000626
OTHER SOURCE(S): MARPAT 134:71905
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Indazole derivs. I [A1 and A2 are certain D- or L-amino acid residues which may be substituted; R1 = amino, alkylamino, arylamino, heteroalkyl, etc.; R2, R3 = H, alkyl, cycloalkyl, cycloalkylalkyl, aryl, heteroalkyl, indanyl, etc. or R2R3N = (un)substituted piperidinyl, piperazinyl, morpholino, or pyrrolidinyl; R4 = (un)substituted aryl, arylalkyl, cycloalkyl, heteroaryl; X = O, S; m = 0-3; n = 1 or 2; p = 0 or 1] were prepared as thrombin receptor antagonists for the treatment of diseases associated with thrombosis, restenosis, hypertension, heart failure, arrhythmia, inflammation, angina, stroke, atherosclerosis, ischemic conditions, angiogenesis related disorders, cancer, and neurodegenerative disorders. Thus, compound II, prepared by a multistep procedure starting from 6-nitroindole (scheme given), showed IC50 = 0.31 and 0.04 μM, resp., in the thrombin-induced gel-filtered platelet aggregation and thrombin receptor binding assays.

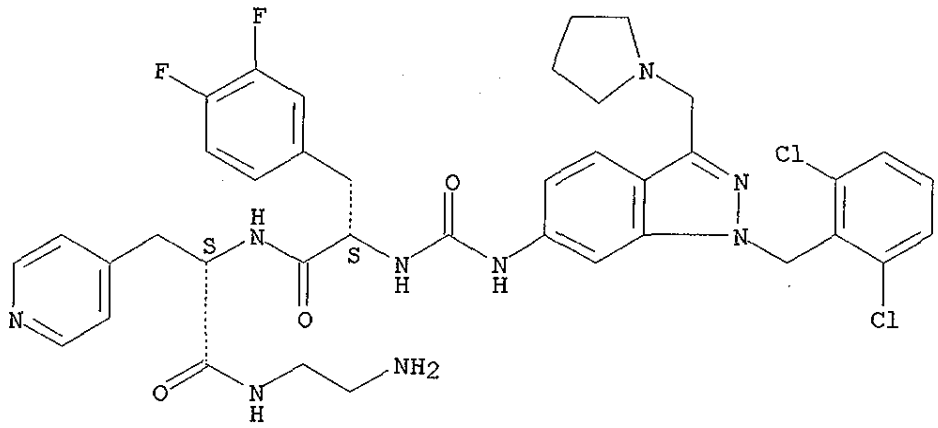
IC ICM C07K005-00
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 28
IT **315203-31-7P** 315203-32-8P **315203-33-9P**
315203-34-0P **315203-35-1P** 315203-36-2P
315203-41-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of indazole peptidomimetics as thrombin receptor antagonists)
IT **315203-31-7P** **315203-33-9P** **315203-34-0P**
315203-35-1P **315203-41-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of indazole peptidomimetics as thrombin receptor antagonists)
RN 315203-31-7 HCAPLUS
CN Benzenepropanamide, N-[(1S)-3-amino-1-[[(phenylmethyl)amino]carbonyl]propyl]-α-[[[[1-[(2,6-dichlorophenyl)methyl]-3-(1-pyrrolidinylmethyl)-1H-indazol-6-yl]amino]carbonyl]amino]-3,4-difluoro-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



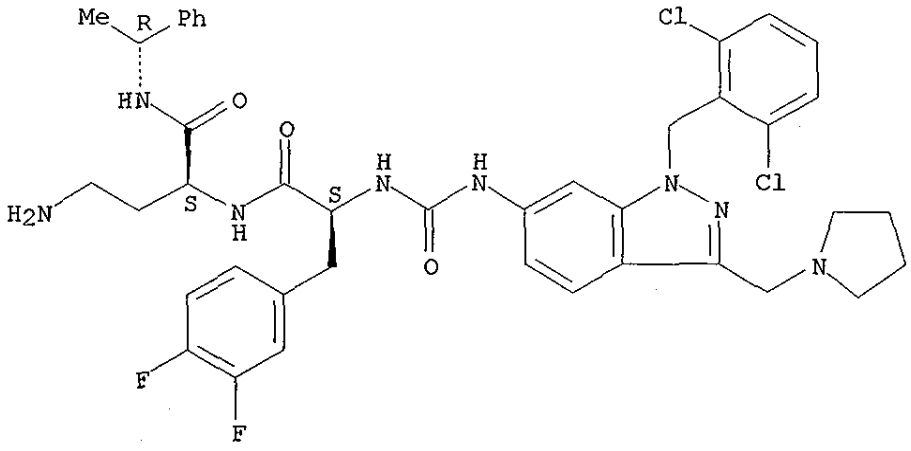
RN 315203-33-9 HCAPLUS
CN L-Alaninamide, N-[[[1-[(2,6-dichlorophenyl)methyl]-3-(1-pyrrolidinylmethyl)-1H-indazol-6-yl]amino]carbonyl]-3,4-difluoro-L-phenylalanyl-N-(2-aminoethyl)-3-(4-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



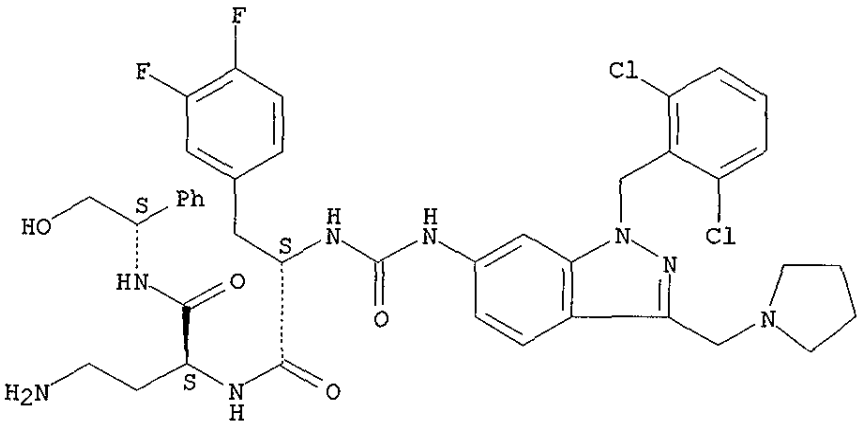
RN 315203-34-0 HCAPLUS
CN Benzenepropanamide, N-[(1S)-3-amino-1-[[[(1R)-1-phenylethyl]amino]carbonyl]propyl]-α-[[[[1-[(2,6-dichlorophenyl)methyl]-3-(1-pyrrolidinylmethyl)-1H-indazol-6-yl]amino]carbonyl]amino]-3,4-difluoro-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



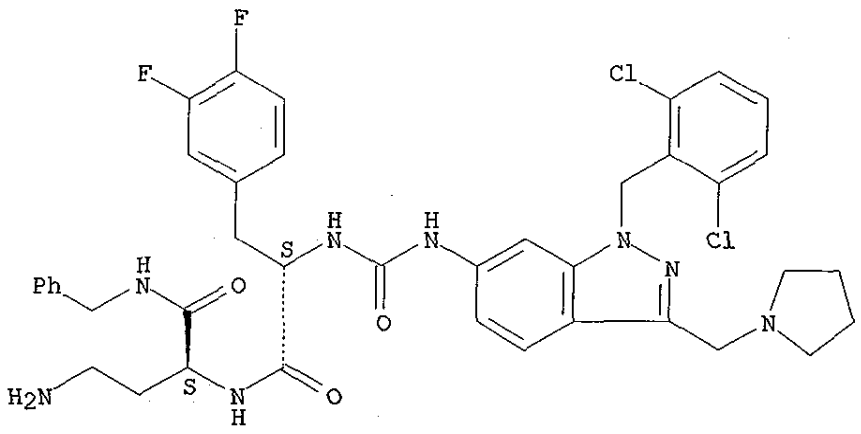
RN 315203-35-1 HCAPLUS
CN Benzenepropanamide, N-[(1S)-3-amino-1-[[[(1S)-2-hydroxy-1-phenylethyl]amino]carbonyl]propyl]-α-[[[[1-[(2,6-dichlorophenyl)methyl]-3-(1-pyrrolidinylmethyl)-1H-indazol-6-yl]amino]carbonyl]amino]-3,4-difluoro-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 315203-41-9 HCAPLUS
CN Benzenepropanamide, N-[(1S)-3-amino-1-[[(phenylmethyl)amino]carbonyl]propyl]-α-[[[[1-[(2,6-dichlorophenyl)methyl]-3-(1-pyrrolidinylmethyl)-1H-indazol-6-yl]amino]carbonyl]amino]-3,4-difluoro-, dihydrochloride, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

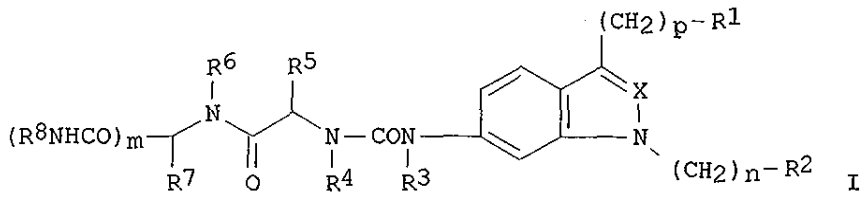


●2 HCl

L6 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:12414 HCAPLUS
DOCUMENT NUMBER: 134:71904
TITLE: Preparation of indole and indazole urea-peptoids as thrombin receptor antagonists
INVENTOR(S): McComsey, David F.; Hoekstra, William J.; Maryanoff, Bruce E.; Zhang, Han-cheng
PATENT ASSIGNEE(S): Ortho-McNeil Pharmaceutical, Inc., USA; Cor Therapeutics, Inc.
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001000576	A1	20010104	WO 2000-US18021	20000629
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6365617	B1	20020402	US 2000-603229	20000626

PRIORITY APPLN. INFO.: US 1999-141555P P 19990629
US 2000-603229 A 20000626
OTHER SOURCE(S): MARPAT 134:71904
GI



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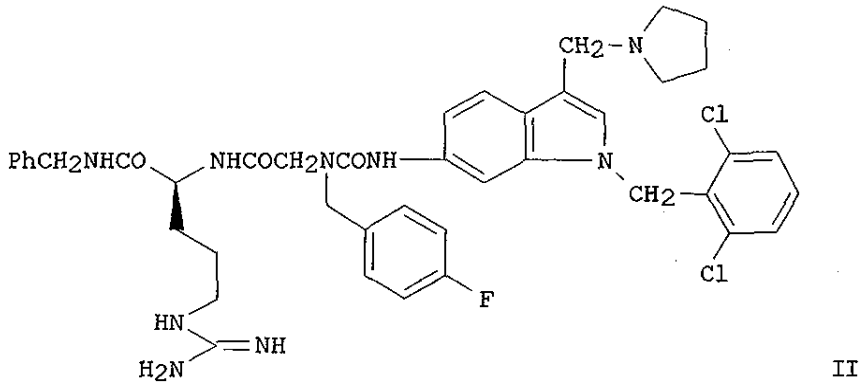


II

AB Indole and indazole urea-peptoid compds. I [R1 = amino, alkylamino, arylamino, heteroalkyl, etc.; R2 = (un)substituted aryl, arylalkyl, cycloalkyl, heteroaryl; R3 = H, alkyl; R4, R5 = H, alkyl, aminoalkyl, aryl, aralkyl, heteroaryl, cycloalkyl, etc.; R6, R7 = H, alkyl, aminoalkyl, aminocycloalkyl, aryl, heteroarylalkyl, etc.; R8 = H, alkyl, aminoalkyl, allyl, cycloalkyl, aryl, heteroaryl, etc.; X = CH, N; n = 0-3; m = 0 or 1; p = 1 or 2] were prepared as thrombin receptor antagonists for the treatment of diseases associated with thrombosis, restenosis, hypertension, heart failure, arrhythmia, inflammation, angina, stroke, atherosclerosis, ischemic conditions, angiogenesis related disorders, cancer, and neurodegenerative disorders. Thus, compound II, prepared by a multistep procedure starting from 6-nitroindole (scheme given), showed IC50 = 1.3 and 0.5 M, resp., in the thrombin-induced gel-filtered platelet aggregation and thrombin receptor binding assays.

IC ICM C07D209-14
ICS C07D231-56; A61K031-4045; A61K031-416; A61P007-02

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 27

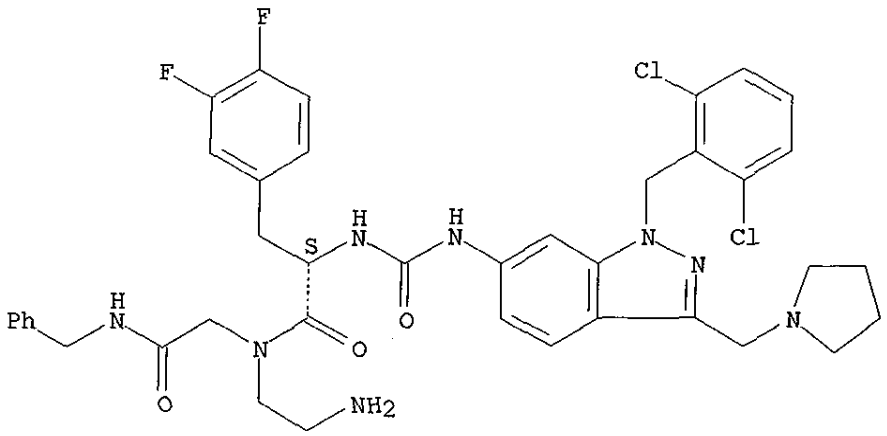
IT **314751-99-0P** 314752-00-6P **314752-01-7P** 314752-02-8P
314752-03-9P 314752-04-0P 314752-05-1P 314752-06-2P
314752-07-3P 314752-08-4P 314752-09-5P 314752-10-8P
314752-11-9P 314752-12-0P 314752-13-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of indole and indazole urea-peptoids as thrombin receptor antagonists)

IT **314751-99-0P 314752-01-7P 314752-07-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of indole and indazole urea-peptoids as thrombin receptor antagonists)

RN 314751-99-0 HCAPLUS

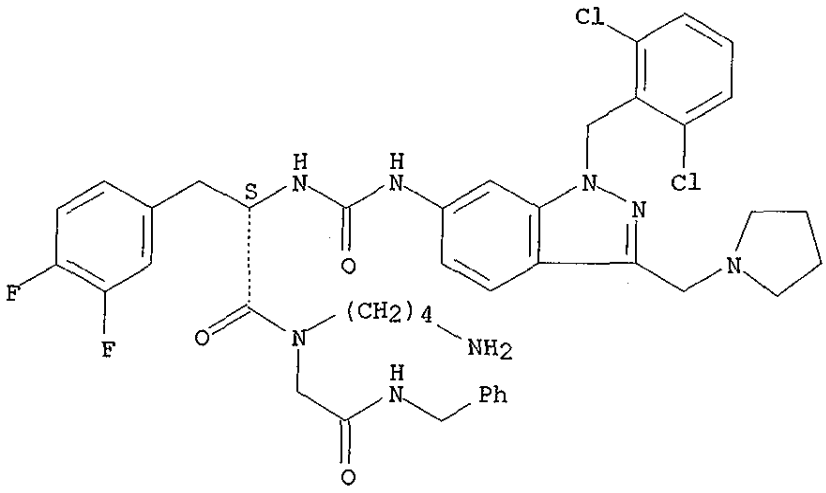
CN Glycinamide, N-[[[1-[(2,6-dichlorophenyl)methyl]-3-(1-pyrrolidinylmethyl)-1H-indazol-6-yl]amino]carbonyl]-3,4-difluoro-L-phenylalanyl-N2-(2-aminoethyl)-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



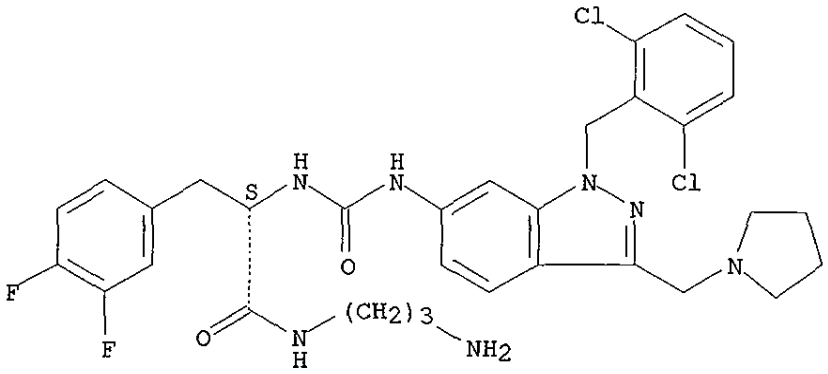
RN 314752-01-7 HCAPLUS
CN Glycinamide, N-[[[1-[(2,6-dichlorophenyl)methyl]-3-(1-pyrrolidinylmethyl)-1H-indazol-6-yl]amino]carbonyl]-3,4-difluoro-L-phenylalanyl-N2-(4-aminobutyl)-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 314752-07-3 HCAPLUS
CN Benzenepropanamide, N-(3-aminopropyl)-α-[[[[1-[(2,6-dichlorophenyl)methyl]-3-(1-pyrrolidinylmethyl)-1H-indazol-6-yl]amino]carbonyl]amino]-3,4-difluoro-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

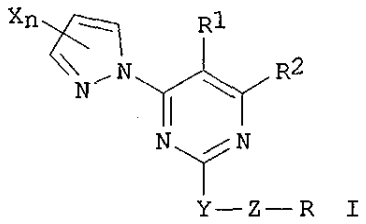


REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 1 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:669444 HCAPLUS
DOCUMENT NUMBER: 137:201325
TITLE: Preparation of pyrazolylpyrimidines as insecticides
INVENTOR(S): Fischer, Ruediger; Alig, Bernd; Bretschneider, Thomas; Es-Sayed, Mazen; Erdelen, Christoph; Loesel, Peter; Reckmann, Udo
PATENT ASSIGNEE(S): Bayer AG, Germany
SOURCE: Ger. Offen., 54 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10108480	A1	20020905	DE 2001-10108480	20010222
WO 2002068413	A1	20020906	WO 2002-EP1400	20020211
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1363905	A1	20031126	EP 2002-711857	20020211
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: DE 2001-10108480 A 20010222
WO 2002-EP1400 W 20020211
OTHER SOURCE(S): MARPAT 137:201325
GI



I

AB Title compds. [I; R1, R2 = H, halo, NO2, cyano, alkyl, haloalkyl, alkoxy, haloalkoxy, alkenyl, alkynyl, alkenyloxy, etc; or R1R2 = (substituted) (O-, S-interrupted) alkylene, alkenylene; X = halo, NO2, cyano, OH, alkyl, haloalkyl, alkoxy, haloalkoxy, alkenyl, alkynyl, alkenyloxy, haloalkenyloxy, alkynyloxy, haloalkynyloxy, etc.; n = 0-3; Y = bond, O, S(O)p, NR9; p = 0-2; R9 = H, alkyl, haloalkyl, cycloalkyl, etc; Z = (CH2)m, (CH2)n(CHR10)(CH2)o, etc.; m = 1-6, n, o = 0-4; R10 = halo, alkyl, alkylcarbonyl, alkoxycarbonyl, cycloalkyl, etc.; R = C(A)E, substituted 5-membered N-containing heterocyclyl; A = O, S, NR15; E = OR16, SR16, etc.; R15 = H, alkyl, alkoxy, cyano, dialkylamino; R16 = H, NR4R5, etc.; R4 = H, alkyl, haloalkyl, cycloalkyl, alkylcarbonyl; R5 = H, amino, COH, alkyl, alkenyl, etc.; or R4R5 = (substituted) alkylidene; NR4R5 = (substituted) (saturated) heterocyclyl, etc.], were prepared Thus, Et a mixture of [(4-chloro-2-pyrimidinyl)thio]acetate (analog preparation given), 5-nitro-1H-pyrazole, and DBU was heated at 140° for 3 min in a microwave apparatus followed by cooling at 70° for 20 min and further heating at 140° for 20 min to give 46% Et [4-(5-nitro-1H-pyrazol-1-yl)-2-pyrimidinyl]thioacetate. I were said to show good insecticidal activity.

IC ICM C07D403-04
ICS C07D403-14; A01N043-56; A01N043-54

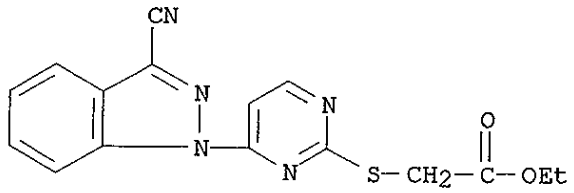
CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 5

IT 452309-66-9P 452309-68-1P 452309-69-2P 452309-71-6P 452309-72-7P
452309-73-8P 452309-74-9P 452309-75-0P 452309-76-1P 452309-77-2P
452309-78-3P 452309-79-4P 452309-80-7P 452309-81-8P 452309-82-9P
452309-83-0P **452309-84-1P** 452309-85-2P 452309-86-3P
452309-87-4P 452309-88-5P 452309-89-6P 452309-90-9P 452309-91-0P
452309-92-1P 452309-93-2P 452309-94-3P 452309-95-4P 452309-96-5P
452309-97-6P 452309-98-7P 452309-99-8P 452310-00-8P 452310-01-9P
452310-02-0P 452310-03-1P 452310-04-2P
RL: AGR (Agricultural use); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrazolylpyrimidines as insecticides)

IT **452309-84-1P**
RL: AGR (Agricultural use); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrazolylpyrimidines as insecticides)

RN 452309-84-1 HCAPLUS

CN Acetic acid, [[4-(3-cyano-1H-indazol-1-yl)-2-pyrimidinyl]thio]-, ethyl ester (9CI) (CA INDEX NAME)



L7 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:241341 HCAPLUS
DOCUMENT NUMBER: 136:257235
TITLE: Indazole peptidomimetic PAR-1 antagonists and PAR-2 antagonists as potential agents for controlling cancer metastasis
INVENTOR(S): D'Andrea, Michael; Derian, Claudia; Woodrow, Hal Brent
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 44 pp., Cont.-in-part of U.S. Ser. No. 603,338.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002037860	A1	20020328	US 2001-865511	20010525
US 2003199455	A1	20031023	US 2003-403218	20030331

PRIORITY APPLN. INFO.: US 1999-141553P P 19990629
US 2000-603338 A2 20000626
OTHER SOURCE(S): MARPAT 136:257235

AB We have discovered a method of modifying the tumor cell microenvironment to reduce or prevent the establishment, growth or metastasis of malignant cells comprising administering to a patient having malignant cells a pharmaceutically effective amount of an indazole peptidomimetic PAR-1 inhibitor and optionally a PAR-2 inhibitor to prevent or reduce activation of normal cells within the tumor microenvironment. This method also has the effect in some patients of modulating the immune system to facilitate a more efficient immune response to malignant cells and maybe coupled with cytokine therapy and T-cell therapy to enhance the patient's immune response to the malignant cells.

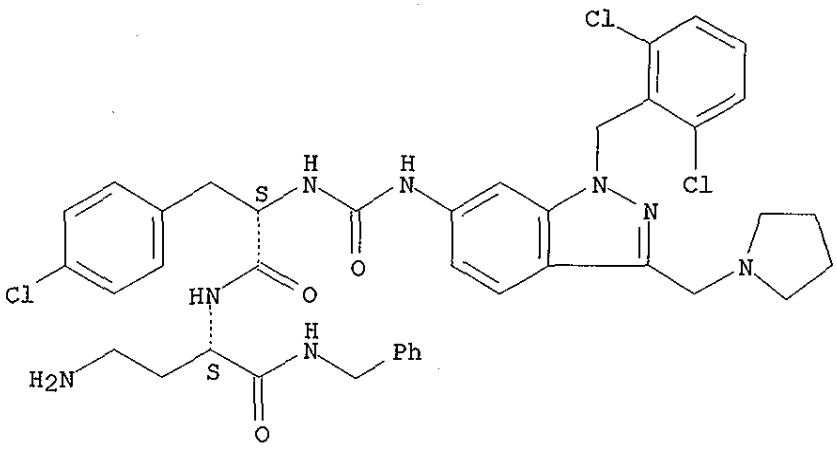
IC ICM A61K038-05
ICS C07D231-56
NCL 514019000
CC 1-6 (Pharmacology)
Section cross-reference(s): 28
IT **315203-32-8DP**, resin-bound 315203-37-3P 315203-38-4P 315203-39-5P 315203-40-8P 315203-42-0P 315203-44-2DP, resin-bound
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(indazole peptidomimetic PAR-1 antagonists and PAR-2 antagonists as potential agents for controlling cancer metastasis)
IT 315203-31-7P **315203-32-8P** 315203-33-9P 315203-34-0P 315203-35-1P **315203-36-2P**

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(indazole peptidomimetic PAR-1 antagonists and PAR-2 antagonists as potential agents for controlling cancer metastasis)

IT **315203-32-8DP**, resin-bound
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(indazole peptidomimetic PAR-1 antagonists and PAR-2 antagonists as potential agents for controlling cancer metastasis)

RN 315203-32-8 HCAPLUS
CN Benzenepropanamide, N-[(1S)-3-amino-1-[[(phenylmethyl)amino]carbonyl]propyl]-4-chloro-α-[[[[1-[(2,6-dichlorophenyl)methyl]-3-(1-pyrrolidinylmethyl)-1H-indazol-6-yl]amino]carbonyl]amino]-, (αS)- (9CI) (CA INDEX NAME)

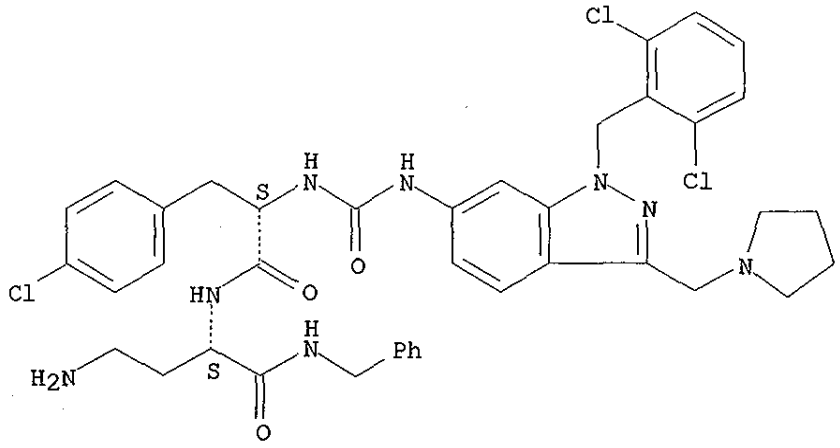
Absolute stereochemistry.



IT **315203-32-8P 315203-36-2P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(indazole peptidomimetic PAR-1 antagonists and PAR-2 antagonists as potential agents for controlling cancer metastasis)

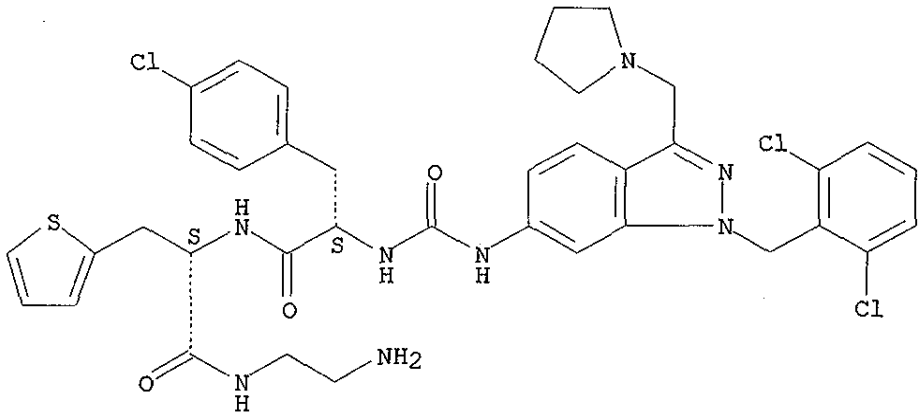
RN 315203-32-8 HCAPLUS
CN Benzenepropanamide, N-[(1S)-3-amino-1-[[(phenylmethyl)amino]carbonyl]propyl]-4-chloro-α-[[[[1-[(2,6-dichlorophenyl)methyl]-3-(1-pyrrolidinylmethyl)-1H-indazol-6-yl]amino]carbonyl]amino]-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 315203-36-2 HCAPLUS
CN L-Alaninamide, 4-chloro-N-[[[1-[(2,6-dichlorophenyl)methyl]-3-(1-pyrrolidinylmethyl)-1H-indazol-6-yl]amino]carbonyl]-L-phenylalanyl-N-(2-aminoethyl)-3-(2-thienyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:12481 HCAPLUS
DOCUMENT NUMBER: 134:71905
TITLE: Preparation of indazole peptidomimetics as thrombin receptor antagonists
INVENTOR(S): Zhang, Han-cheng; Maryanoff, Bruce E.; Pandey, Anjali; Scarborough, Robert M.
PATENT ASSIGNEE(S): Ortho-Mcneil Pharmaceutical, Inc., USA; Cor Therapeutics, Inc.
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001000656	A2	20010104	WO 2000-US17718	20000628
WO 2001000656	A3	20010525		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2003199455	A1	20031023	US 2003-403218	20030331
PRIORITY APPLN. INFO.:			US 1999-141553P	P 19990629
			US 2000-603338	A 20000626

OTHER SOURCE(S): MARPAT 134:71905
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Indazole derivs. I [A1 and A2 are certain D- or L-amino acid residues which may be substituted; R1 = amino, alkylamino, arylamino, heteroalkyl, etc.; R2, R3 = H, alkyl, cycloalkyl, cycloalkylalkyl, aryl, heteroalkyl, indanyl, etc. or R2R3N = (un)substituted piperidinyl, piperazinyl, morpholino, or pyrrolidinyl; R4 = (un)substituted aryl, arylalkyl, cycloalkyl, heteroaryl; X = O, S; m = 0-3; n = 1 or 2; p = 0 or 1] were prepared as thrombin receptor antagonists for the treatment of diseases associated with thrombosis, restenosis, hypertension, heart failure, arrhythmia, inflammation, angina, stroke, atherosclerosis, ischemic conditions, angiogenesis related disorders, cancer, and neurodegenerative disorders. Thus, compound II, prepared by a multistep procedure starting from 6-nitroindole (scheme given), showed IC50 = 0.31 and 0.04 μM, resp., in the thrombin-induced gel-filtered platelet aggregation and thrombin receptor binding assays.

IC ICM C07K005-00
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 28

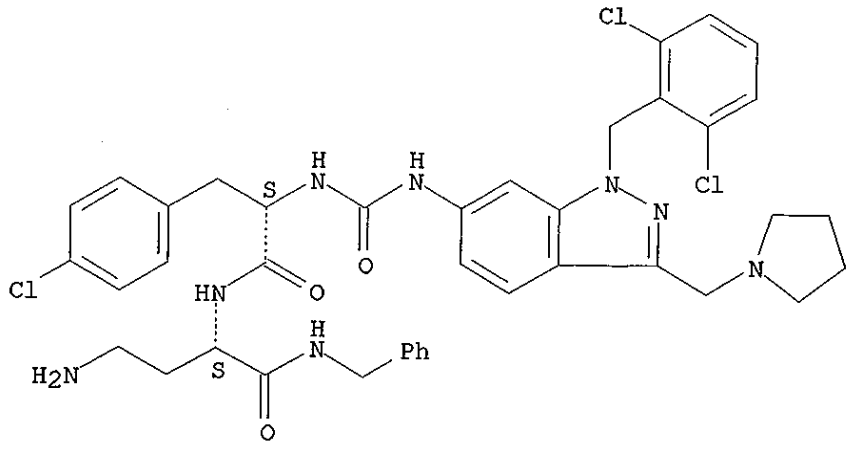
IT 315203-31-7P **315203-32-8P** 315203-33-9P 315203-34-0P
315203-35-1P **315203-36-2P** 315203-41-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of indazole peptidomimetics as thrombin receptor antagonists)

IT **315203-32-8P 315203-36-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of indazole peptidomimetics as thrombin receptor antagonists)

RN 315203-32-8 HCAPLUS
CN Benzenepropanamide, N-[(1S)-3-amino-1-[[(phenylmethyl)amino]carbonyl]propyl]-4-chloro-α-[[[[1-[(2,6-dichlorophenyl)methyl]-3-(1-pyrrolidinylmethyl)-1H-indazol-6-yl]amino]carbonyl]amino]-, (αS)-

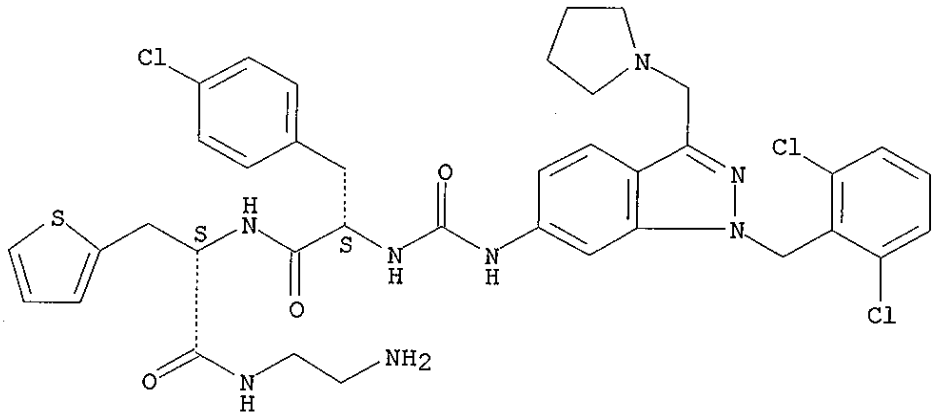
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 315203-36-2 HCAPLUS
CN L-Alaninamide, 4-chloro-N-[[[1-[(2,6-dichlorophenyl)methyl]-3-(1-pyrrolidinylmethyl)-1H-indazol-6-yl]amino]carbonyl]-L-phenylalanyl-N-(2-aminoethyl)-3-(2-thienyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:708753 HCAPLUS
DOCUMENT NUMBER: 131:322912
TITLE: Preparation of substituted amino acid diarylalkyl amides as calcium channel antagonists
INVENTOR(S): Connor, Davis Thomas; Hu, Lain-yen; Malone, Thomas Charles; Rafferty, Michael Francis; Roth, Bruce David; Ryder, Todd Robert; Sercel, Anthony Denver; Song, Yuntao
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 151 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9955688	A1	19991104	WO 1999-US7133	19990331
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9934599	A1	19991116	AU 1999-34599	19990331
US 6458781	B1	20021001	US 1999-403579	19991025

PRIORITY APPLN. INFO.: US 1998-83141P P 19980427
WO 1999-US7133 W 19990331

OTHER SOURCE(S): MARPAT 131:322912

AB Amides R1R2NCR3R4-Y-X-CHR5R6 [X = NH(CH2)n (n = 0-6), 1,4-piperazinediyl; Y = CO, CH2; R1, R2 = H, alkyl, alkenyl, alkoxycarbonyl, (CH2)nPh or ring-substituted derivs., CO2CH2Ph, cycloalkyl-(CH2)n, heterocyclyl-(CH2)n, CONZ2, where Z2 = (CH2)nNR7(CH2)n (R7 = alkyl, Ph, heterocycloalkyl) or (CH2)n or R1R2N = heterocycloalkyl; R3 = H, alkyl, (un)substituted Ph or benzyl, (CH2)ncycloalkyl; R4 = H, alkyl or R3 and R4 form a cycloalkyl ring; R5, R6 = (un)substituted phenyl] were prepared as calcium channels blockers. Thus, (S)-azepane-1-carboxylic acid [1-[[4,4-bis(4-fluorophenyl)butyl]carbamoyl]-3-methylbutyl]amide, prepared by amidation of (S)-2-[(azepane-1-carbonyl)amino]-4-methylpentanoic acid with 4,4-bis(4-fluorophenyl)butylamine hydrochloride, showed IC50 = 0.820 μM for Ca2+ channel blocking potency in IMR-32 cells.

IC ICM C07D295-20
ICS C07C271-20; C07C237-20; C07D209-34; C07D231-56; C07D295-18; C07C237-06; A61K031-16; A61K031-445; A61K031-55; C07D295-12

CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1

IT
248921-57-5P	248921-58-6P	248921-59-7P	248921-60-0P	248921-61-1P
248921-64-4P	248921-65-5P	248921-68-8P	**248921-69-9P**	
248921-71-3P	248921-72-4P	248921-74-6P	248921-75-7P	248921-77-9P
248921-78-0P	248921-79-1P	248921-80-4P	248921-81-5P	248921-82-6P
248921-83-7P	248921-85-9P	248921-86-0P	248921-87-1P	248921-88-2P
248921-89-3P	248921-91-7P	248921-92-8P	248921-93-9P	248921-94-0P
248921-95-1P	248921-96-2P	248921-98-4P	248921-99-5P	248922-00-1P
248922-01-2P	248922-02-3P	248922-03-4P	248922-04-5P	248922-06-7P
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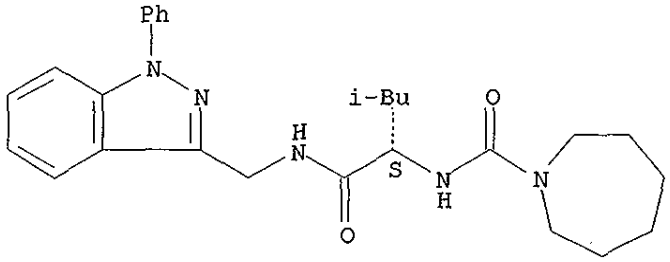
248922-59-0P	248922-60-3P	248922-61-4P	248922-62-5P	248922-63-6P
248922-64-7P	248922-65-8P	248922-66-9P	248922-67-0P	248922-68-1P
248922-69-2P	248922-70-5P	248922-72-7P	248922-73-8P	248922-74-9P

248922-75-0P 248922-76-1P 248922-77-2P 248922-78-3P 248922-79-4P
248922-80-7P 248922-81-8P 248927-05-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted amino acid diarylalkyl amides as calcium channel antagonists)

IT **248921-69-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted amino acid diarylalkyl amides as calcium channel antagonists)

RN 248921-69-9 HCAPLUS
CN 1H-Azepine-1-carboxamide, hexahydro-N-[(1S)-3-methyl-1-[[[(1-phenyl-1H-indazol-3-yl)methyl]amino]carbonyl]butyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:42394 HCAPLUS
DOCUMENT NUMBER: 128:102084
TITLE: Preparation of 4-heterocyclyl-1-piperidineacetates as glycoprotein IIb/IIIa receptor antagonists
INVENTOR(S): Allen, David George; Eldred, Colin David; Judkins, Brian David; Mitchell, William Leonard; Scopes, David Ian Carter
PATENT ASSIGNEE(S): Glaxo Group Ltd., UK; Allen, David George; Eldred, Colin David; Judkins, Brian David; Mitchell, William Leonard; Scopes, David Ian Carter
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

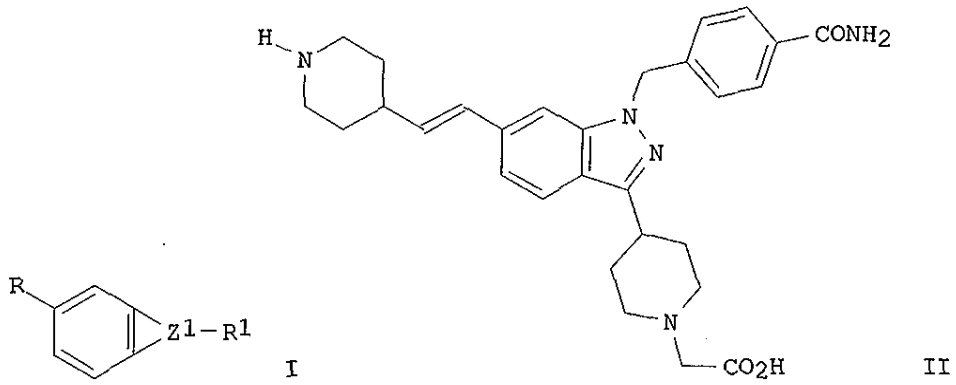
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9749698	A1	19971231	WO 1997-EP3194	19970619

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US,

UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9732610	A1	19980114	AU 1997-32610		19970619
ZA 9705431	A	19981221	ZA 1997-5431		19970619
CN 1222153	A	19990707	CN 1997-195652		19970619
PRIORITY APPLN. INFO.:			GB 1996-13017	A	19960621
			GB 1996-13018	A	19960621
			GB 1996-13026	A	19960621
			GB 1996-13095	A	19960621
			WO 1997-EP3194	W	19970619

OTHER SOURCE(S): MARPAT 128:102084
GI



I II

AB Title compds. [I; R = Z2R2; R1 = Z3CHR3CO2H; R2 = piperidinyl, piperazinyl, quinuclidinyl; R3 = H, alkyl, (hetero)aryl, etc.; Z1 = atoms to complete an (un)substituted R1-substituted heterocyclic ring; Z2 = CH2CH2, CH:CH, C.tplbond.C; Z3 = piperidine-4,1-diyl] were prepared Thus, 3-BrC6H4Br was acylated by 1-acetylpiperidine-4-carbonyl chloride and the hydrazone of the deprotected product cyclized to give I (R = Br, R1 = 4-piperidinyl, Z1 = C:NNH) which was N-alkylated by BrCH2CO2CMe3 to give, in 2 addnl. steps, title compound II. Data for biol. activity of I were given.

IC ICM C07D401-14
ICS A61K031-415; A61K031-41; A61K031-445; C07D413-14; C07D453-02

CC 28-8 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

IT

201227-06-7P	201227-07-8P	201227-08-9P	201227-09-0P	201227-10-3P
201227-12-5P	201227-29-4P	201482-18-0P	201482-19-1P	201482-20-4P
201482-21-5P	201482-22-6P	201482-23-7P	201482-24-8P	201482-25-9P
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201483-09-2P 201483-10-5P 201483-12-7P 201483-13-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 4-heterocyclyl-1-piperidineacetates as glycoprotein IIb/IIIa receptor antagonists)

IT 34774-91-9P 180307-50-0P 180307-51-1P 180307-52-2P 180307-54-4P
180307-58-8P 180307-61-3P 201227-16-9P, 5-Bromo-2-nitro-1H-indazole
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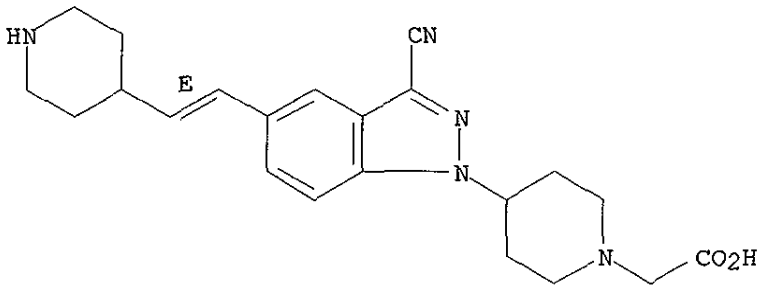
201483-64-9P 201483-66-1P 201483-67-2P 201483-68-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 4-heterocyclyl-1-piperidineacetates as glycoprotein IIb/IIIa receptor antagonists)

IT **201482-94-2P 201482-95-3P 201482-98-6P**
201482-99-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 4-heterocyclyl-1-piperidineacetates as glycoprotein IIb/IIIa receptor antagonists)

RN 201482-94-2 HCAPLUS
CN 1-Piperidineacetic acid, 4-[3-cyano-5-[2-(4-piperidinyl)ethenyl]-1H-indazol-1-yl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

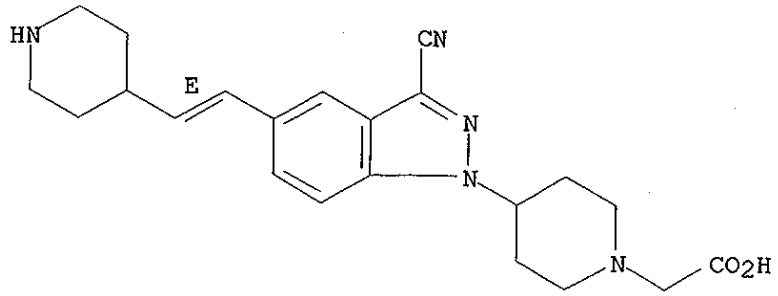


RN 201482-95-3 HCAPLUS
CN 1-Piperidineacetic acid, 4-[3-cyano-5-[2-(4-piperidinyl)ethenyl]-1H-indazol-1-yl]-, (E)-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

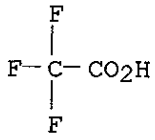
CRN 201482-94-2
CMF C22 H27 N5 O2

Double bond geometry as shown.

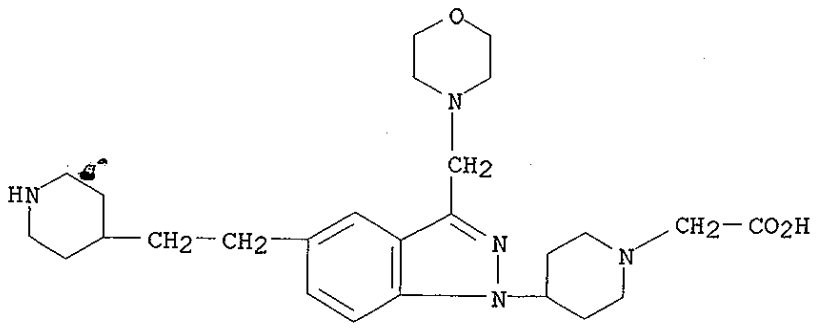


CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 201482-98-6 HCAPLUS
CN 1-Piperidineacetic acid, 4-[3-(4-morpholinylmethyl)-5-[2-(4-piperidinyl)ethyl]-1H-indazol-1-yl]- (9CI) (CA INDEX NAME)

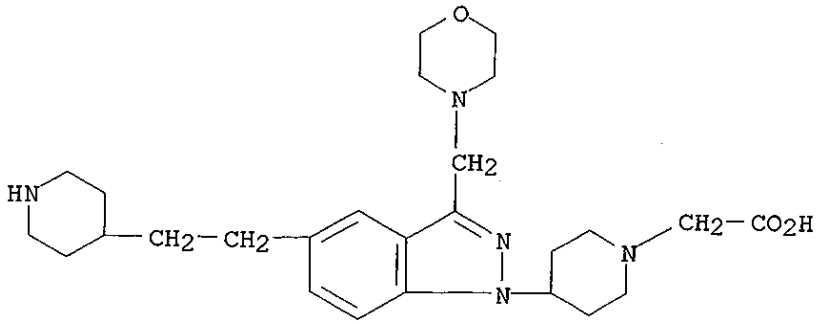


RN 201482-99-7 HCAPLUS
CN 1-Piperidineacetic acid, 4-[3-(4-morpholinylmethyl)-5-[2-(4-

piperidinyl)ethyl]-1H-indazol-1-yl]-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

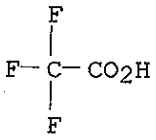
CM 1

CRN 201482-98-6
CMF C26 H39 N5 O3



CM 2

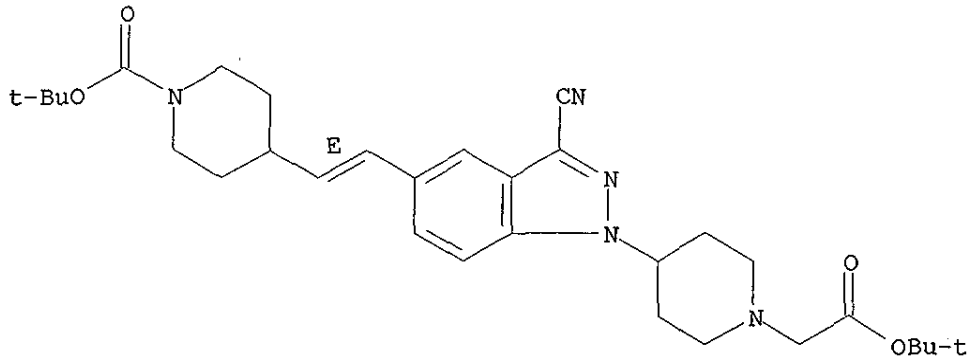
CRN 76-05-1
CMF C2 H F3 O2



IT **201483-56-9P 201483-62-7P 201483-63-8P**
201483-64-9P 201483-66-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 4-heterocyclyl-1-piperidineacetates as glycoprotein IIb/IIIa receptor antagonists)

RN 201483-56-9 HCAPLUS
CN 1-Piperidineacetic acid, 4-[3-cyano-5-[2-[1-[(1,1-dimethylethoxy)carbonyl]-4-piperidinyl]ethenyl]-1H-indazol-1-yl]-, 1,1-dimethylethyl ester, (E)- (9CI) (CA INDEX NAME)

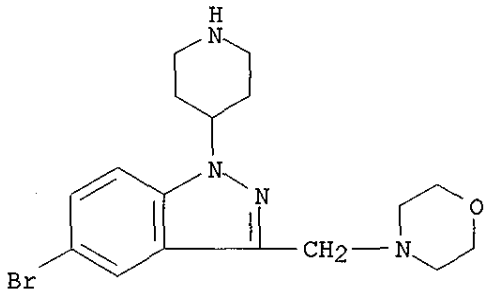
Double bond geometry as shown.



RN 201483-62-7 HCAPLUS
CN 1H-Indazole, 5-bromo-3-(4-morpholinylmethyl)-1-(4-piperidinyl)-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

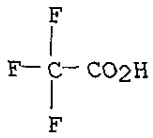
CM 1

CRN 201483-61-6
CMF C17 H23 Br N4 O

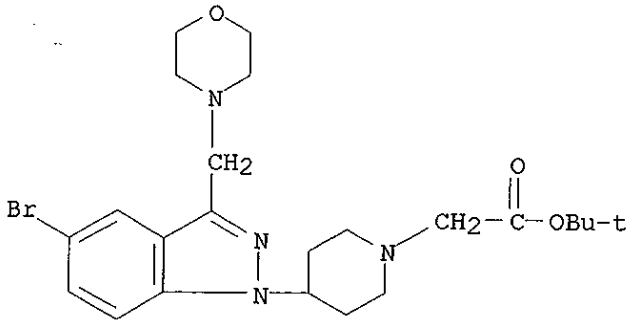


CM 2

CRN 76-05-1
CMF C2 H F3 O2

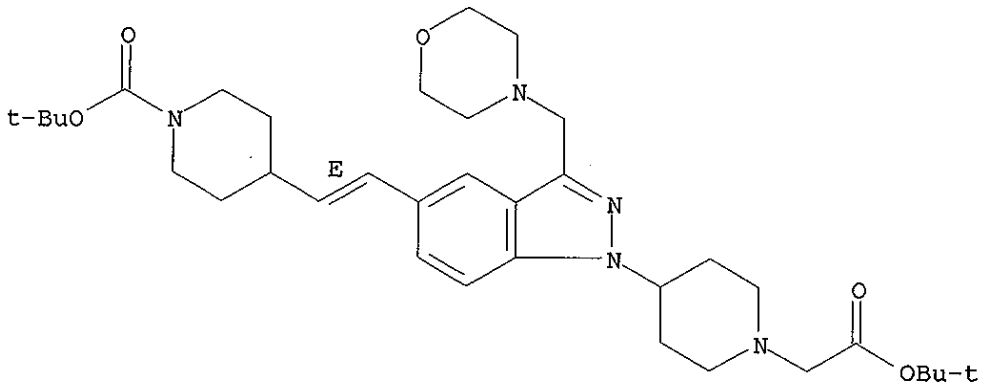


RN 201483-63-8 HCAPLUS
CN 1-Piperidineacetic acid, 4-[5-bromo-3-(4-morpholinylmethyl)-1H-indazol-1-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 201483-64-9 HCAPLUS
CN 1-Piperidineacetic acid, 4-[5-[2-[1-[(1,1-dimethylethoxy)carbonyl]-4-piperidinyl]ethenyl]-3-(4-morpholinylmethyl)-1H-indazol-1-yl]-, 1,1-dimethylethyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

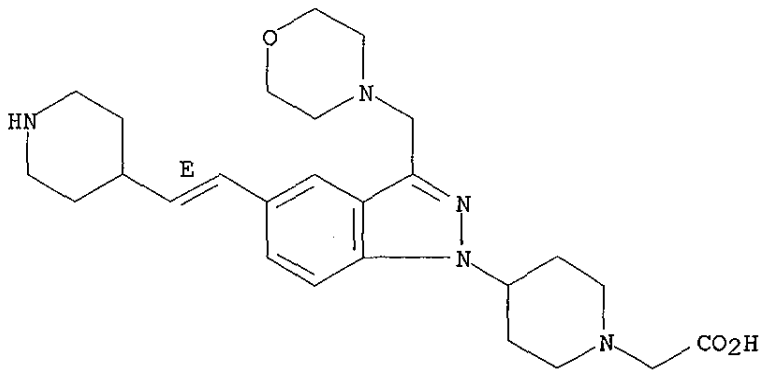


RN 201483-66-1 HCAPLUS
CN 1-Piperidineacetic acid, 4-[3-(4-morpholinylmethyl)-5-[2-(4-piperidinyl)ethenyl]-1H-indazol-1-yl]-, (E)-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

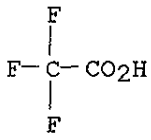
CRN 201483-65-0
CMF C26 H37 N5 O3

Double bond geometry as shown.



CM 2

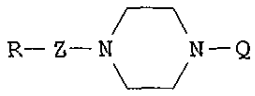
CRN 76-05-1
CMF C2 H F3 O2



L7 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:701490 HCAPLUS
DOCUMENT NUMBER: 128:22921
TITLE: Preparation of piperazines having calmodulin inhibitory activity
INVENTOR(S): Yamamoto, Kenjiro; Hasegawa, Atsushi; Kubota, Hideki; Andodeceased, Masahiro; Yamaguchi, Hitoshi
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan
SOURCE: U.S., 44 pp., Cont.-in-part of U.S. Ser. No. 242,842, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5681954	A	19971028	US 1995-416311	19950404
PRIORITY APPLN. INFO.:			JP 1993-11277	19930514
			US 1994-242842	19940516

OTHER SOURCE(S): MARPAT 128:22921
GI



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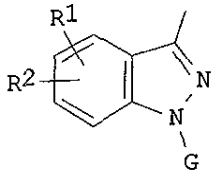
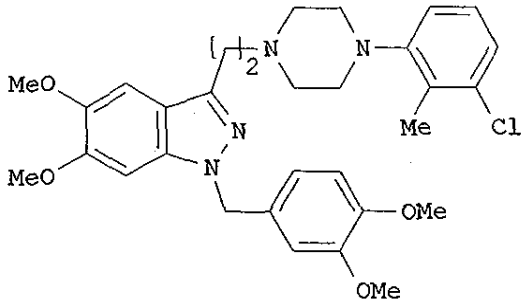
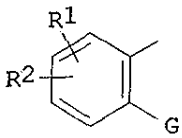


II



IV



III

AB The title compds. [I; Q = C1-6 alkyl, C1-6 alkoxy, CF3, etc.; R = II or III (wherein G = C1-6 alkyl, (un)substituted Ph, etc.; R1, R2 = C1-6 alkyl, C1-6 alkoxy, CF3, etc.); Z = C1-3 alkylene, C2-4 alkenylene, C(O), etc.], useful as a treating agent for diseases in the circulatory organs or in the cerebral region which are caused by excessive activation of calmodulin, were prepared Thus, treatment of 1-{[5,6-dimethoxy-1-(3,4-dimethoxybenzyl)-1H-indazol-3-yl]acetyl}-4-(3-chloro-2-methylphenyl)piperazine with BH3*THF in THF afforded the title compound IV which showed 19.2% increase of survival time on nitrogen-induced hypoxia model in mouse, and IC50 of 3.1 against calmodulin-dependent PDE.

IC ICM C07D413-00

NCL 544114000

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

IT 1245-28-9P 4293-90-7P 160521-92-6P 160521-93-7P 162495-33-2P
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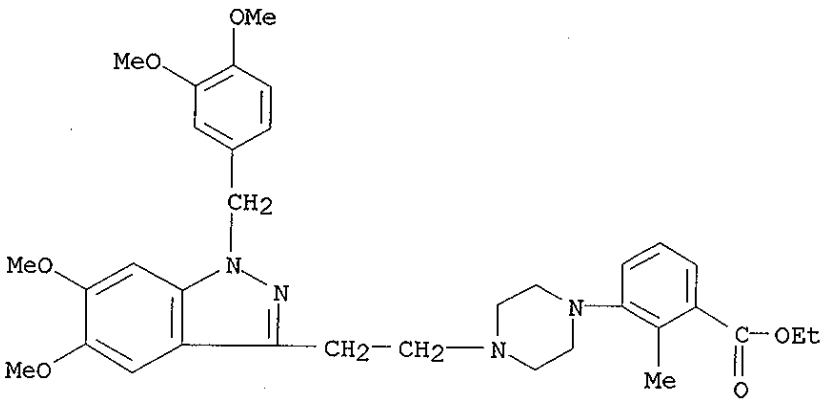
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazines having calmodulin inhibitory activity)

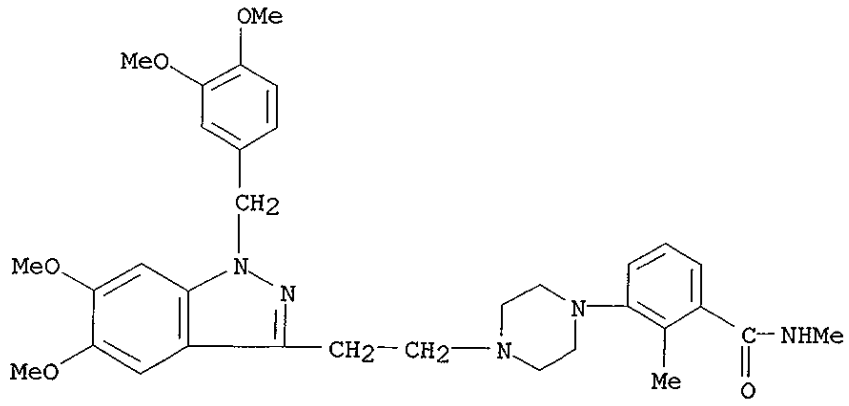
IT **183315-09-5P 183315-17-5P 183315-41-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazines having calmodulin inhibitory activity)

RN 183315-09-5 HCAPLUS
CN Benzoic acid, 3-[4-[2-[1-[(3,4-dimethoxyphenyl)methyl]-5,6-dimethoxy-1H-indazol-3-yl]ethyl]-1-piperazinyl]-2-methyl-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

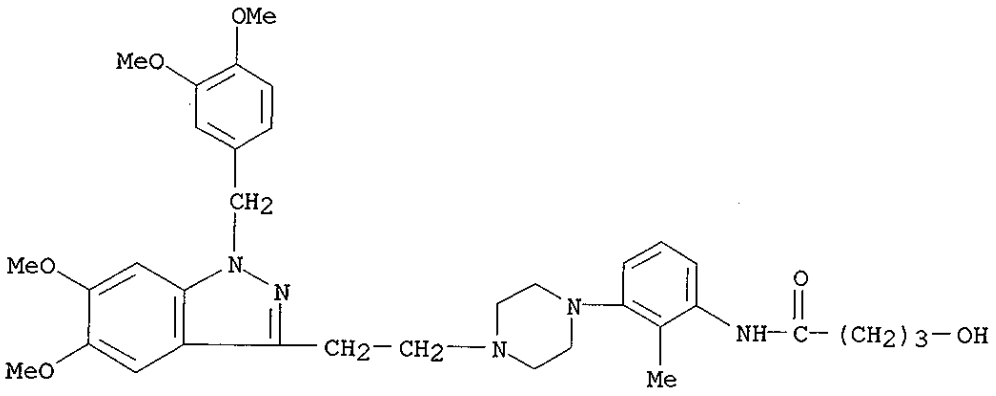


● HCl

RN 183315-17-5 HCAPLUS
CN Benzamide, 3-[4-[2-[1-[(3,4-dimethoxyphenyl)methyl]-5,6-dimethoxy-1H-indazol-3-yl]ethyl]-1-piperazinyl]-N,2-dimethyl- (9CI) (CA INDEX NAME)



RN 183315-41-5 HCAPLUS
CN Butanamide, N-[3-[4-[2-[1-[(3,4-dimethoxyphenyl)methyl]-5,6-dimethoxy-1H-indazol-3-yl]ethyl]-1-piperazinyl]-2-methylphenyl]-4-hydroxy- (9CI) (CA INDEX NAME)



L7 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:513631 HCAPLUS
DOCUMENT NUMBER: 127:205572
TITLE: Preparation of thiazolylbenzofurans as leukotriene and SRS-A antagonists or inhibitors
INVENTOR(S): Matsuo, Masaaki; Okumura, Kazuo; Shigenaga, Shinji; Nishimura, Hiroaki; Matsuda, Hiroshi; Hagiwara, Daijiro; Terasaka, Tadashi
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan; Matsuo, Masaaki; Okumura, Kazuo; Shigenaga, Shinji; Nishimura, Hiroaki; Matsuda, Hiroshi; Hagiwara, Daijiro; Terasaka, Tadashi
SOURCE: PCT Int. Appl., 244 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9727190	A1	19970731	WO 1997-JP73	19970117
W: AU, CA, CN, HU, JP, KR, MX, SG, US, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
ZA 9700415	A	19970730	ZA 1997-415	19970117
CA 2244189	AA	19970731	CA 1997-2244189	19970117
AU 9713991	A1	19970820	AU 1997-13991	19970117
EP 880519	A1	19981202	EP 1997-900432	19970117
EP 880519	B1	20020417		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
CN 1209809	A	19990303	CN 1997-191798	19970117
JP 2000503984	T2	20000404	JP 1997-526720	19970117
EP 1170009	A2	20020109	EP 2001-123263	19970117
EP 1170009	A3	20020116		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
TW 474811	B	20020201	TW 1997-86100473	19970117
AT 216384	E	20020515	AT 1997-900432	19970117
ES 2171878	T3	20020916	ES 1997-900432	19970117
US 5994378	A	19991130	US 1998-101766	19980721

PRIORITY APPLN. INFO.:

GB 1996-1235	A	19960122
AU 1996-1111	A	19960718
AU 1996-9241	A	19960412
EP 1997-900432	A3	19970117
WO 1997-JP73	W	19970117

OTHER SOURCE(S): MARPAT 127:205572

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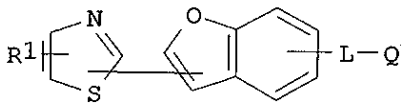

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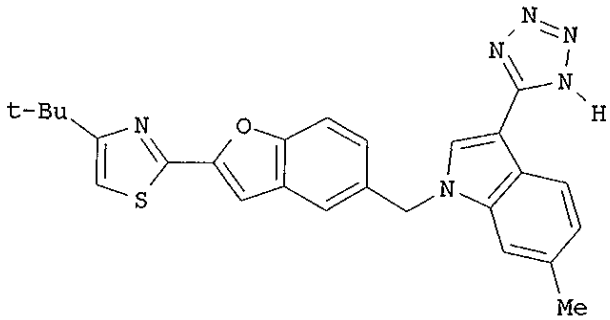

II

AB The title compds. [I; R1 = lower alkyl; L = single bond, (un)substituted lower alkylene; Q = (un)substituted heterocyclic group, lower alkoxy substituted with aryl] which possess activities as leukotriene and SRS-A antagonists or inhibitors, and are useful in the treatment and/or prevention of allergy or inflammation, were prepared Thus, treatment of

4-tert-butyl-2-{5-[(3-cyano-6-methylindol-1-yl)methyl]benzofuran-2-yl}thiazole with NaN3 and NH4Cl in DMF afforded the title compound II which showed IC50 of < 5 nM against 3H-leukotriene D4 receptor binding.

IC ICM C07D417-04
ICS A61K031-42; C07D417-14

CC 28-7 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

IT 194486-71-0P 194486-73-2P 194486-80-1P 194486-81-2P 194486-82-3P
194486-84-5P 194486-85-6P 194486-86-7P 194486-89-0P 194486-94-7P
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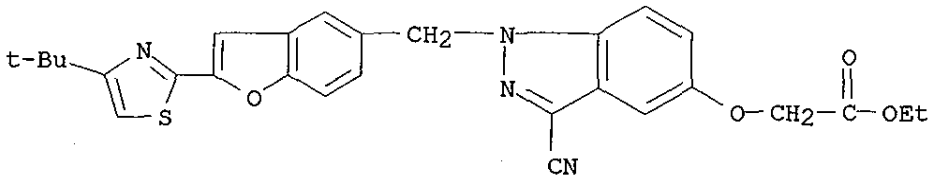
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of thiazolylbenzofurans as leukotriene and SRS-A antagonists or inhibitors)

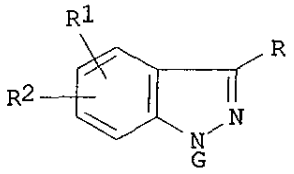
IT **194488-08-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of thiazolylbenzofurans as leukotriene and SRS-A antagonists or inhibitors)
RN 194488-08-9 HCAPLUS
CN Acetic acid, [[3-cyano-1-[[2-[4-(1,1-dimethylethyl)-2-thiazolyl]-5-benzofuranyl]methyl]-1H-indazol-5-yl]oxy]-, ethyl ester (9CI) (CA INDEX NAME)



L7 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:694212 HCAPLUS
DOCUMENT NUMBER: 125:328730
TITLE: Preparation of 3-(piperazinoalkyl)indole derivatives as calmodulin antagonists
INVENTOR(S): Hasegawa, Atsushi; Makino, Tooru; Yamamoto, Kenjiro
PATENT ASSIGNEE(S): Daiichi Seiyaku Co, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 49 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08225535	A2	19960903	JP 1995-294071	19951113

PRIORITY APPLN. INFO.: JP 1994-280963 19941115
OTHER SOURCE(S): MARPAT 125:328730
GI



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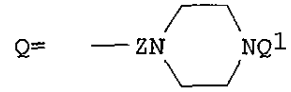

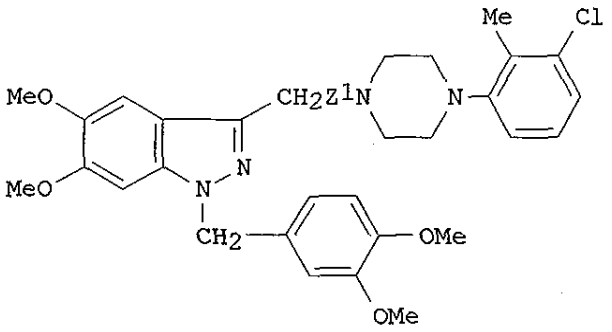

II

AB The title compds. [I; R = Q; wherein Z = single bond, C1-3 alkylene, C2-4 alkenylene, C1-3 hydroxyalkylene, CO, COCO, C1-2 alkylene containing one CO group at the end or middle of the C chain; Q1 = C1-8 alkyl, C3-8 cycloalkyl, (un)substituted aryl, heterocyclyl, diarylmethyl, or aryl-C1-6 alkyl; R1, R2 = C1-6 alkyl or alkoxy, CF3, CF3CH2, CF3O, CF3CH2O, C1-6 alkylthio, alkylsulfinyl, or alkylsulfonyl, C1-6 alkylcarbonyl, C2-7 alkanoylamino, NH2, mono- di(C1-6 alkyl)amino, OH, halo, C2-6 perfluoroalkyl, cyano, NO2, CO2H, C1-6 alkoxycarbonyl, tetrazolyl, SO2NH2, methylenedioxy, ethylenedioxy, morpholinosulfonyl, piperazinosulfonyl, 4-(C1-6 alkyl)piperazinosulfonyl, 4-[mono- or di(C1-6 alkyl)amino]piperidino, 4-aminopiperidino; G = C1-6 alkyl, (un)substituted Ph, PhCO, PhCOCH2, α-hydroxybenzyl, phenyl-C1-6 alkyl, 5-membered aromatic heterocyclyl or heterocyclyl-C1-6 alkyl containing heteroatoms (a) N, O,

or S or (b) one or two N and another N, O, or S, 6-membered aromatic heterocyclyl, heterocyclylcarbonyl, or heterocyclyl-C1-3 alkyl containing one or two N, phenylhydroxyalkyl, or 2-phenylethynyl, tetrazolyl, morpholino, etc.] are prepared These compds. possess calmodulin-inhibitory, antihypoxic, or brain edema-improving activity, inhibit delayed neuronal death in hippocampus, and are useful for the treatment of circulatory diseases or brain diseases. Thus, 5,6-dimethoxy-1-(3,4-dimethoxybenzyl)-1H-indazole-3-acetic acid was condensed with 1-(3-chloro-2-methylphenyl)piperazine using di(2-pyridyl) disulfide and Ph3P in CH2Cl2 at room temperature to give an intermediate (II; Z1 = CO), which was reduced by borane-THF complex in THF under reflux to give the title compound II (Z1 = CH2). The latter compound in vitro showed IC50 of 3.1 μg/mL against Ca/calmodulin-dependent phosphodiesterase.

IC ICM C07D231-56
ICS C07D401-06; C07D401-12; C07D401-14; C07D403-06; C07D403-12; C07D405-06; C07D405-12; C07D405-14; C07D417-06; C07D491-048; C07D491-056
ICA A61K031-415; A61K031-495; A61K031-505
ICI C07D401-06, C07D213-16, C07D231-56; C07D401-12, C07D213-16
CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1

IT 160521-92-6P 160521-93-7P 160522-00-9P 162495-46-7P 162495-48-9P
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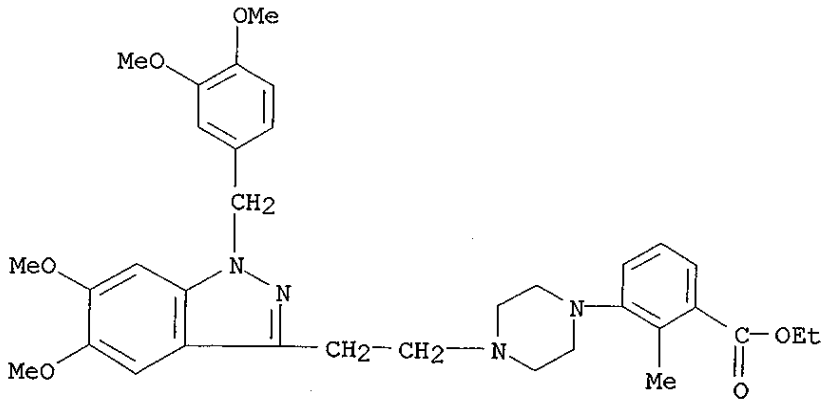
183315-75-5P **183315-76-6P 183315-77-7P**
183315-78-8P 183315-79-9P **183315-80-2P**
183315-81-3P 183315-82-4P 183315-83-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3-(piperazinoalkyl)indole derivs. as calmodulin antagonists for disease treatment)

IT **183315-09-5P 183315-17-5P 183315-41-5P**
183315-57-3P 183315-58-4P 183315-59-5P
183315-60-8P 183315-67-5P 183315-72-2P
183315-73-3P 183315-76-6P 183315-77-7P
183315-78-8P 183315-80-2P 183315-81-3P
183315-82-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3-(piperazinoalkyl)indole derivs. as calmodulin antagonists for disease treatment)

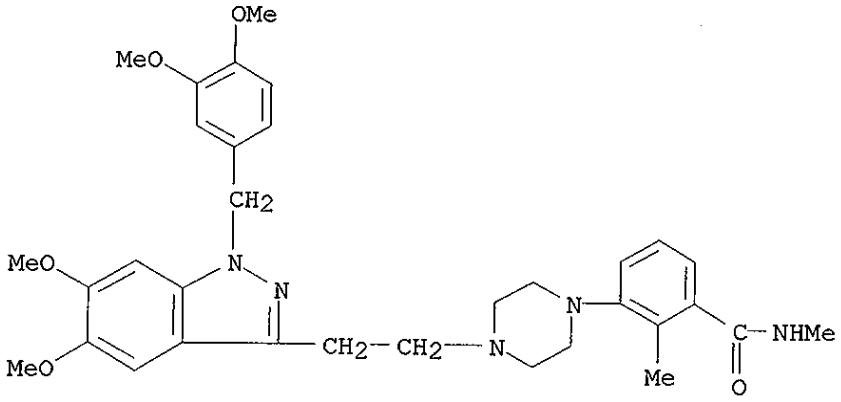
RN 183315-09-5 HCAPLUS

CN Benzoic acid, 3-[4-[2-[1-[(3,4-dimethoxyphenyl)methyl]-5,6-dimethoxy-1H-indazol-3-yl]ethyl]-1-piperazinyl]-2-methyl-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

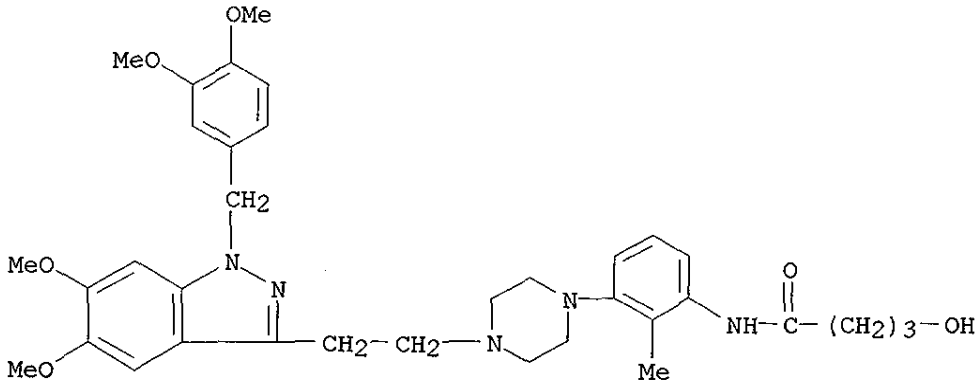


● HCl

RN 183315-17-5 HCAPLUS
CN Benzamide, 3-[4-[2-[1-[(3,4-dimethoxyphenyl)methyl]-5,6-dimethoxy-1H-indazol-3-yl]ethyl]-1-piperazinyl]-N,2-dimethyl- (9CI) (CA INDEX NAME)

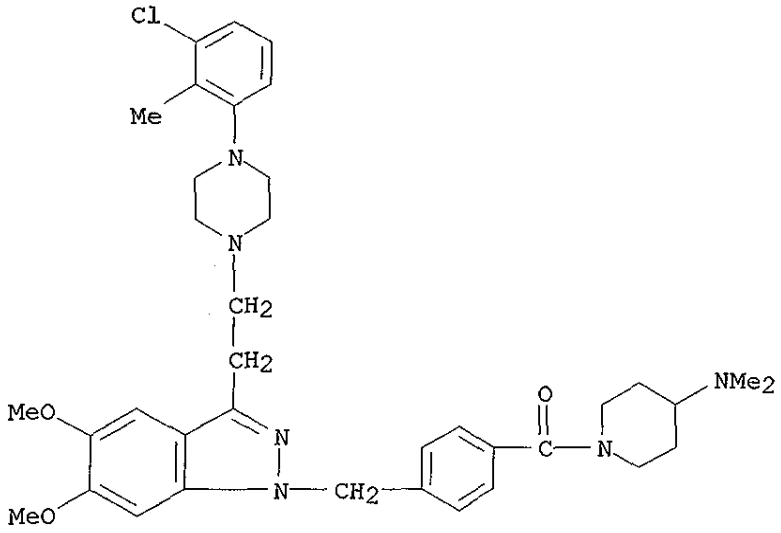


RN 183315-41-5 HCAPLUS
CN Butanamide, N-[3-[4-[2-[1-[(3,4-dimethoxyphenyl)methyl]-5,6-dimethoxy-1H-indazol-3-yl]ethyl]-1-piperazinyl]-2-methylphenyl]-4-hydroxy- (9CI) (CA INDEX NAME)



RN 183315-57-3 HCAPLUS
CN 4-Piperidinamine, 1-[4-[[3-[2-[4-(3-chloro-2-methylphenyl)-1-piperazinyl]ethyl]-5,6-dimethoxy-1H-indazol-1-yl]methyl]benzoyl]-N,N-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)

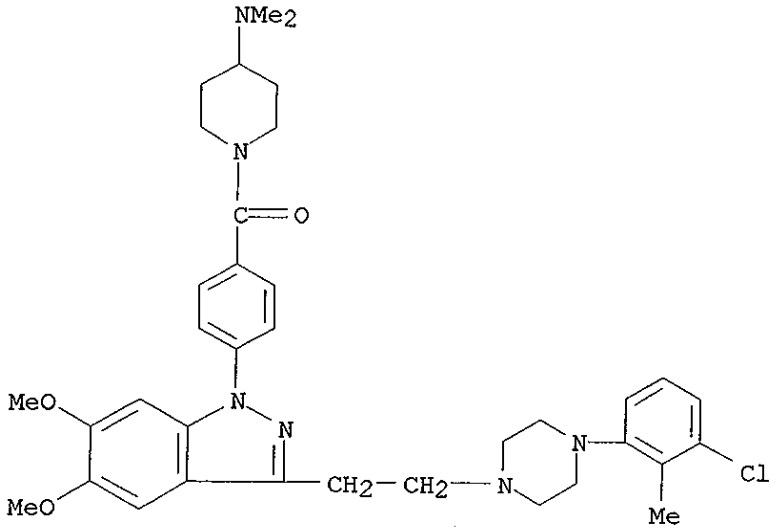
PAGE 1-A



PAGE 2-A

RN 183315-58-4 HCAPLUS
CN 4-Piperidinamine, 1-[4-[3-[2-[4-(3-chloro-2-methylphenyl)-1-piperazinyl]ethyl]-5,6-dimethoxy-1H-indazol-1-yl]benzoyl]-N,N-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)

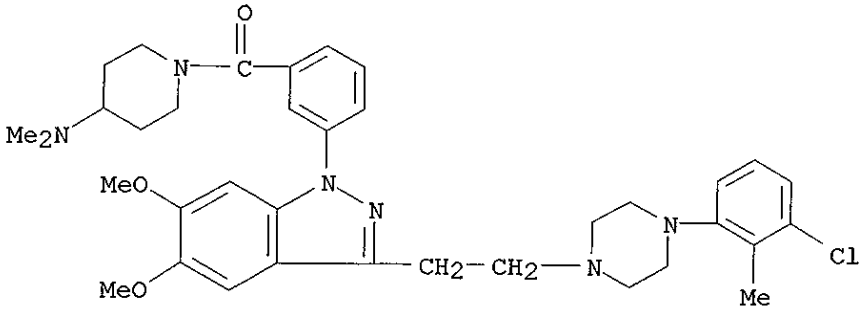
PAGE 1-A



PAGE 2-A

●2 HCl

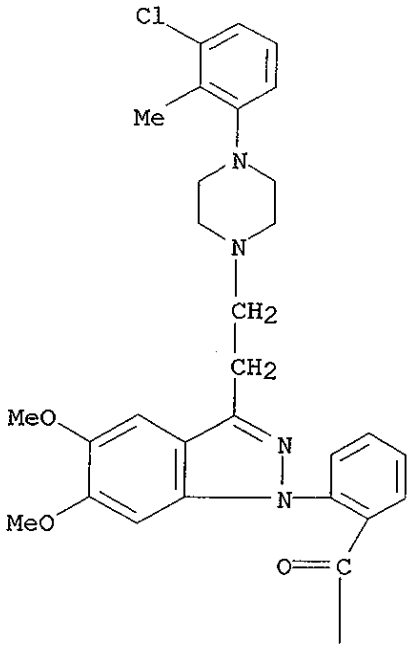
RN 183315-59-5 HCAPLUS
CN 4-Piperidinamine, 1-[3-[3-[2-[4-(3-chloro-2-methylphenyl)-1-piperazinyl]ethyl]-5,6-dimethoxy-1H-indazol-1-yl]benzoyl]-N,N-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 183315-60-8 HCAPLUS
CN 4-Piperidinamine, 1-[2-[3-[2-[4-(3-chloro-2-methylphenyl)-1-piperazinyl]ethyl]-5,6-dimethoxy-1H-indazol-1-yl]benzoyl]-N,N-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



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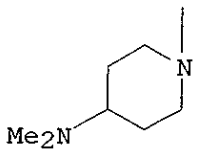
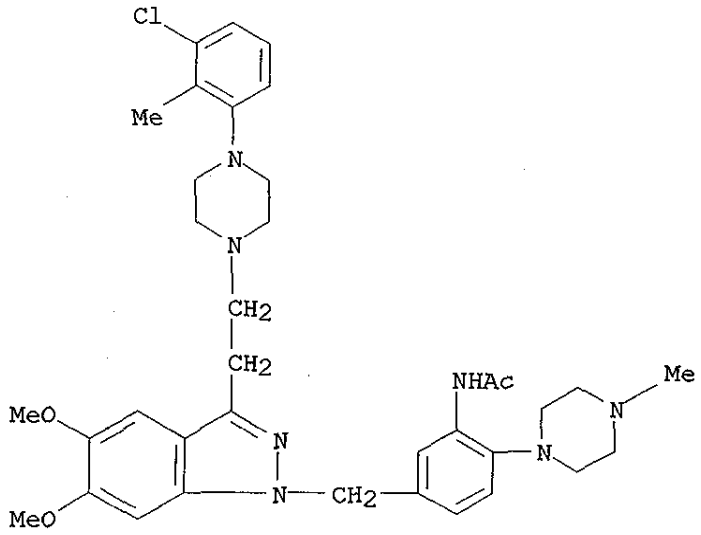


●2 HCl

RN 183315-67-5 HCAPLUS
CN Acetamide, N-[5-[[3-[2-[4-(3-chloro-2-methylphenyl)-1-piperazinyl]ethyl]-5,6-dimethoxy-1H-indazol-1-yl]methyl]-2-(4-methyl-1-piperazinyl)phenyl]-, dihydrochloride (9CI) (CA INDEX NAME)

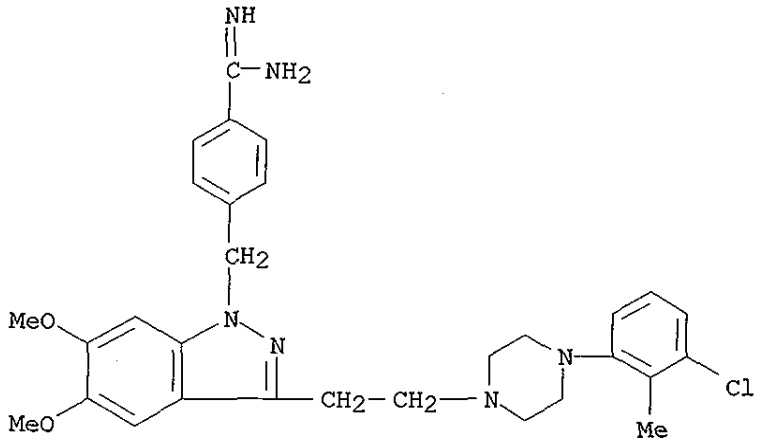
PAGE 1-A



PAGE 2-A

●2 HCl

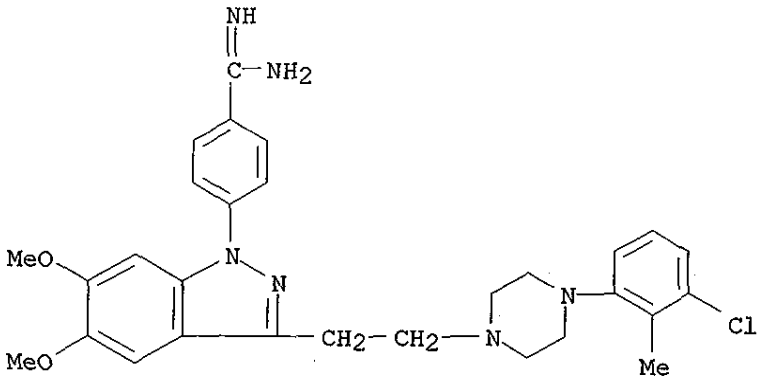
RN 183315-72-2 HCAPLUS
CN Benzenecarboximidamide, 4-[[3-[2-[4-(3-chloro-2-methylphenyl)-1-piperazinyl]ethyl]-5,6-dimethoxy-1H-indazol-1-yl]methyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

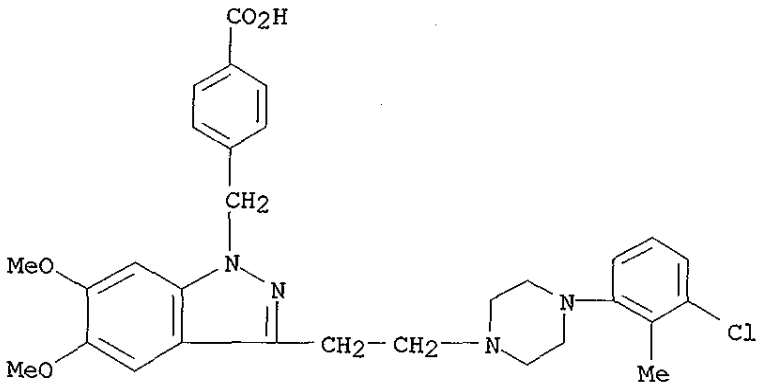
RN 183315-73-3 HCAPLUS

CN Benzenecarboximidamide, 4-[3-[2-[4-(3-chloro-2-methylphenyl)-1-piperazinyl]ethyl]-5,6-dimethoxy-1H-indazol-1-yl]-, monohydrochloride (9CI) (CA INDEX NAME)



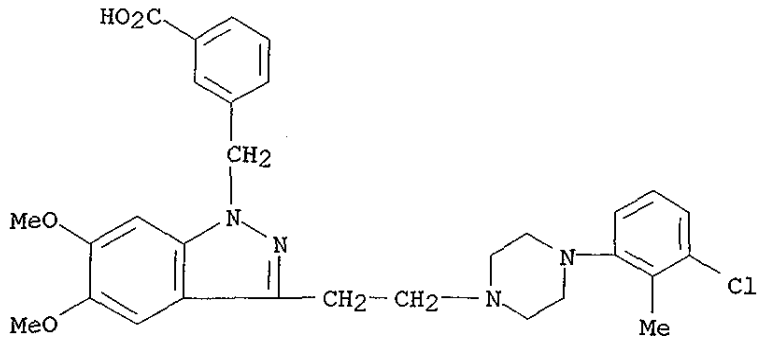
● HCl

RN 183315-76-6 HCAPLUS
CN Benzoic acid, 4-[[3-[2-[4-(3-chloro-2-methylphenyl)-1-piperazinyl]ethyl]-5,6-dimethoxy-1H-indazol-1-yl]methyl]-, sodium salt (9CI) (CA INDEX NAME)

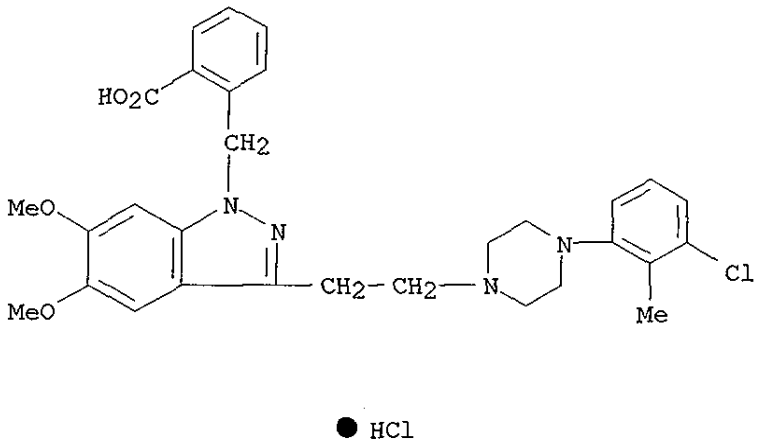


● Na

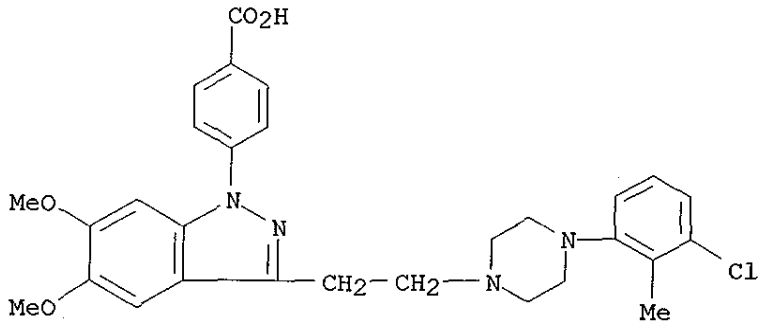
RN 183315-77-7 HCAPLUS
CN Benzoic acid, 3-[[3-[2-[4-(3-chloro-2-methylphenyl)-1-piperazinyl]ethyl]-5,6-dimethoxy-1H-indazol-1-yl]methyl]- (9CI) (CA INDEX NAME)



RN 183315-78-8 HCAPLUS
CN Benzoic acid, 2-[[3-[2-[4-(3-chloro-2-methylphenyl)-1-piperazinyl]ethyl]-5,6-dimethoxy-1H-indazol-1-yl]methyl]-, monohydrochloride (9CI) (CA INDEX NAME)

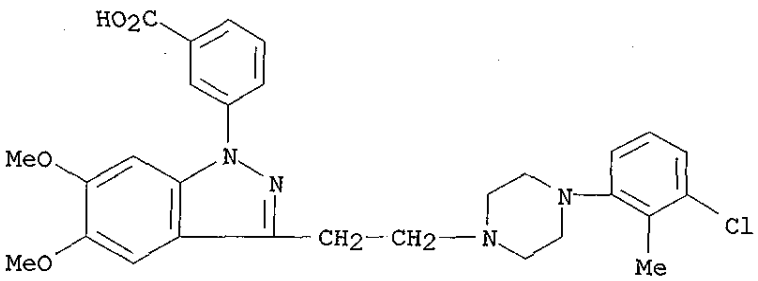


RN 183315-80-2 HCAPLUS
CN Benzoic acid, 4-[3-[2-[4-(3-chloro-2-methylphenyl)-1-piperazinyl]ethyl]-5,6-dimethoxy-1H-indazol-1-yl]-, hydrochloride (2:1) (9CI) (CA INDEX NAME)



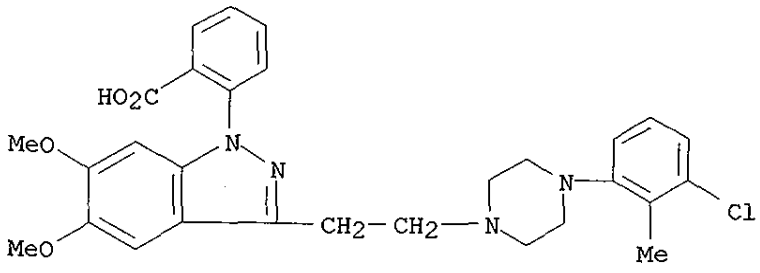
●1/2 HCl

RN 183315-81-3 HCAPLUS
CN Benzoic acid, 3-[3-[2-[4-(3-chloro-2-methylphenyl)-1-piperazinyl]ethyl]-5,6-dimethoxy-1H-indazol-1-yl]-, hydrochloride (3:1) (9CI) (CA INDEX NAME)



●1/3 HCl

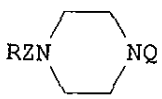
RN 183315-82-4 HCAPLUS
CN Benzoic acid, 2-[3-[2-[4-(3-chloro-2-methylphenyl)-1-piperazinyl]ethyl]-5,6-dimethoxy-1H-indazol-1-yl]- (9CI) (CA INDEX NAME)



L7 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:507921 HCAPLUS
DOCUMENT NUMBER: 123:55919
TITLE: Preparation of piperazine derivatives as calmodulin inhibitors.
INVENTOR(S): Yamamoto, Kenjiro; Hasegawa, Atsushi; Kubota, Hideki; Ando, Masahiro; Yamaguchi, Hitoshi C. O. Daiichi
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co. Ltd., Japan
SOURCE: Eur. Pat. Appl., 70 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 624584	A1	19941117	EP 1994-107496	19940513
EP 624584	B1	19980819		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, PT, SE				
RU 2124511	C1	19990110	RU 1994-16183	19940512
CA 2123548	AA	19941115	CA 1994-2123548	19940513
CA 2123548	C	20030408		
FI 9402252	A	19941115	FI 1994-2252	19940513
NO 9401802	A	19941115	NO 1994-1802	19940513
AU 9463096	A1	19941117	AU 1994-63096	19940513
AU 677644	B2	19970501		
CN 1101039	A	19950405	CN 1994-105810	19940513
CN 1049654	B	20000223		
JP 07097364	A2	19950411	JP 1994-99391	19940513
JP 3220591	B2	20011022		
AT 169914	E	19980915	AT 1994-107496	19940513
ES 2125372	T3	19990301	ES 1994-107496	19940513
JP 2002053553	A2	20020219	JP 2001-178197	19940513
TW 418198	B	20010111	TW 1994-83104731	19940525
AU 9724952	A1	19970904	AU 1997-24952	19970617
AU 698486	B2	19981029		

PRIORITY APPLN. INFO.: JP 1993-112771 A 19930514
JP 1994-99391 A3 19940513
OTHER SOURCE(S): MARPAT 123:55919
GI



I

AB Title compds. I (Q = aryl, heterocyclyl, diarylmethyl, aralkyl composed of an aryl and an alkylene having C1-6, C1-8 alkyl, C3-8 cycloalkyl, in which the aryl, heterocyclyl, and the aryl moiety of the diarylmethyl and aralkyl may be substituted, etc.; R = bicyclic N-containing heterocyclyl, (substituted) Ph, etc.; Z = C1-3 alkylene, C2-4 alkenylene, HO-C1-3 alkylene, CO, etc.) or salt thereof, are prepared I R =

5,6-dimethoxy-1-(3,4-dimethoxybenzyl)-1H-indazol-3-yl, Z = CH2CO, Q = 2,3-ClMeC6H3 (preparation given) in THF and borane-THF complex were refluxed for 2 h to give I (R = 5,6-dimethoxy-1-(3,4-dimethoxybenzyl)-1H-indazol-3-yl, Z = CH2CH2, Q = 2,3-ClMeC6H3). Calmodulin inhibitory activity was demonstrated.

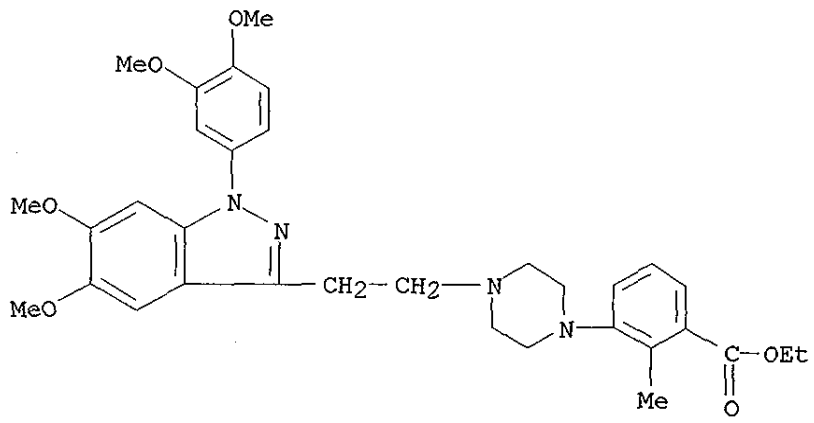
IC ICM C07D403-08
ICS A61K031-495; C07D403-14; C07D405-14; C07D413-14; C07D241-04; C07D405-10; C07D409-10

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

IT 1245-28-9P 160521-93-7P 160521-99-3P 160522-00-9P 162477-42-1P
162477-43-2P 162495-30-9P 162495-31-0P 162495-32-1P 162495-33-2P
162495-34-3P 162495-35-4P 162495-36-5P 162495-37-6P 162495-38-7P
162495-39-8P 162495-40-1P 162495-41-2P 162495-42-3P 162495-43-4P
162495-44-5P 162495-45-6P 162495-46-7P 162495-47-8P 162495-48-9P
162495-49-0P 162495-50-3P 162495-51-4P 162495-52-5P 162495-53-6P
162495-54-7P 162495-55-8P 162495-56-9P 162495-57-0P 162495-58-1P
162495-59-2P 162495-60-5P 162495-61-6P 162495-62-7P 162495-63-8P
162495-64-9P 162495-65-0P 162495-66-1P 162495-67-2P 162495-68-3P
162495-69-4P 162495-70-7P **162495-71-8P** 162495-72-9P
162495-73-0P 162495-74-1P 162495-75-2P 162495-76-3P 162495-77-4P
162495-78-5P **162495-79-6P** 162495-80-9P 162495-81-0P
162495-82-1P 162495-83-2P 162495-84-3P 162495-85-4P 162495-86-5P
162495-87-6P 162495-88-7P 162495-89-8P 162495-90-1P 162495-91-2P
162495-92-3P 162495-93-4P 162495-94-5P 162495-95-6P 162495-96-7P
162495-97-8P 162495-98-9P 162495-99-0P 162496-00-6P 162496-01-7P
162496-02-8P 162496-03-9P 162496-04-0P **162496-05-1P**
162496-06-2P 162496-07-3P 162496-08-4P 162496-09-5P 162496-10-8P
162496-11-9P 162496-12-0P 162496-13-1P 162496-14-2P 162496-15-3P
162496-16-4P 162496-17-5P 162496-18-6P 162496-19-7P 162496-20-0P
162496-22-2P 162496-23-3P 162496-24-4P 162496-25-5P 162496-26-6P
162496-27-7P 162496-28-8P 162496-29-9P 162496-30-2P 162496-31-3P
162496-32-4P 162496-33-5P 162496-34-6P 162496-35-7P 162496-36-8P
162496-37-9P 162496-38-0P 162496-39-1P 162496-40-4P 162496-41-5P
162496-42-6P 162496-43-7P 162496-44-8P 162496-45-9P 162496-71-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazine derivs. as calmodulin inhibitors.)

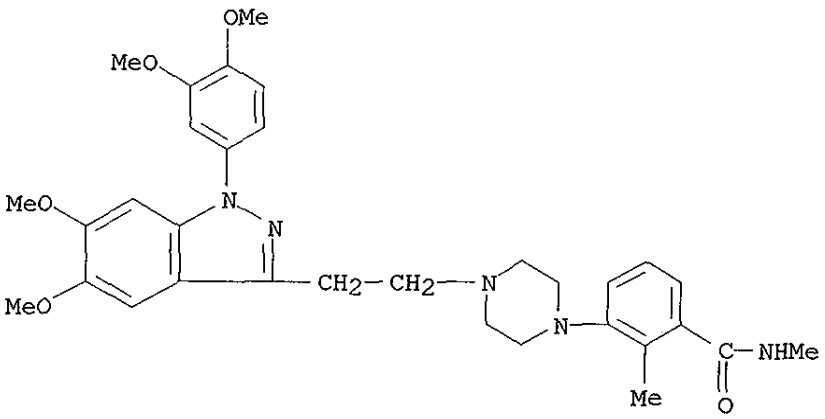
IT **162495-71-8P 162495-79-6P 162496-05-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazine derivs. as calmodulin inhibitors.)

RN 162495-71-8 HCAPLUS
CN Benzoic acid, 3-[4-[2-[1-(3,4-dimethoxyphenyl)-5,6-dimethoxy-1H-indazol-3-yl]ethyl]-1-piperazinyl]-2-methyl-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

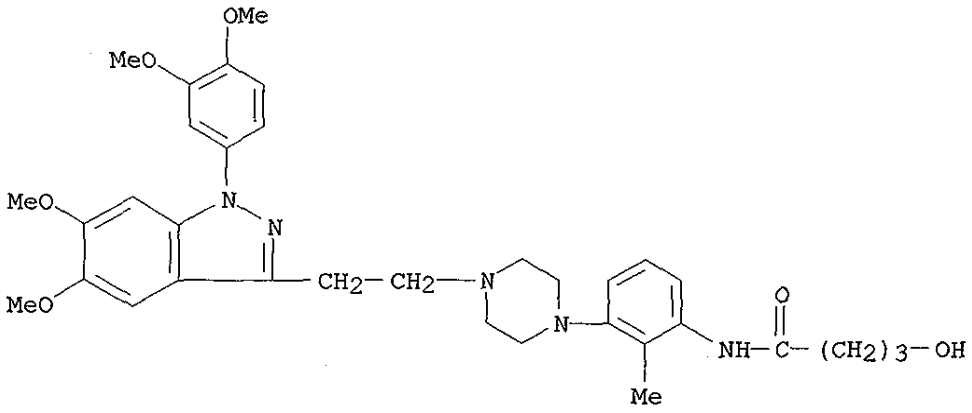


● HCl

RN 162495-79-6 HCAPLUS
CN Benzamide, 3-[4-[2-[1-(3,4-dimethoxyphenyl)-5,6-dimethoxy-1H-indazol-3-yl]ethyl]-1-piperazinyl]-N,2-dimethyl- (9CI) (CA INDEX NAME)



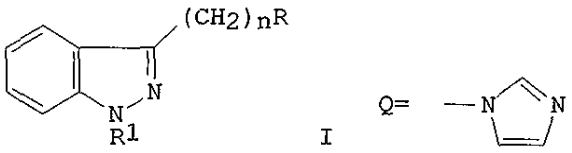
RN 162496-05-1 HCAPLUS
CN Butanamide, N-[3-[4-[2-[1-(3,4-dimethoxyphenyl)-5,6-dimethoxy-1H-indazol-3-yl]ethyl]-1-piperazinyl]-2-methylphenyl]-4-hydroxy- (9CI) (CA INDEX NAME)



L7 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1987:102275 HCAPLUS
DOCUMENT NUMBER: 106:102275
TITLE: Indazole derivatives
INVENTOR(S): Kanao, Soji; Watanabe, Yoshifumi
PATENT ASSIGNEE(S): Daiichi Seiyaku Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

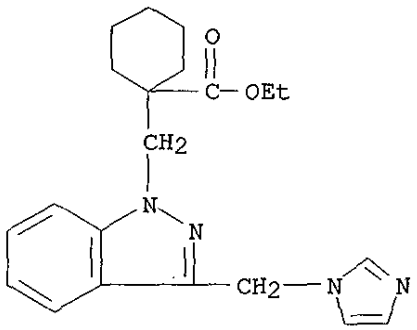
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 61100580	A2	19860519	JP 1984-221902	19841024
JP 04021673	B4	19920413		

PRIORITY APPLN. INFO.: JP 1984-221902 19841024
GI



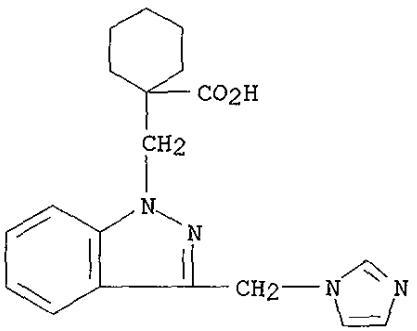
AB The title compds. (I; R = Q; R1 = H, substituted aryl, substituted alkyl; n = 1-3) were prepared Thus, reaction of I (R = Cl; R1 = H; n = 1) with AcQ and the addition reaction of the resulting I (R = Q; R1 = H; n = 1) with CH2:CHCN in 40% Triton B/MeOH gave I (R = Q; R1 = CH2CH2CN; n = 1), whose hydrolysis gave I (R = Q; R1 = CH2CH2CO2H; n = 1). I at 2.0-20 μM selectively inhibited the synthesis of thromboxane A2 in vitro in rat blood-plasma containing 5 + 108 platelets/mL. I are useful as drugs for heart attack, cardiac infarction, coronary thrombosis, cerebral thrombosis, etc.
IC ICM C07D403-06

ICA A61K031-415; C07D231-56
ICI C07D403-06, C07D231-00, C07D233-00
CC 28-8 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
IT 105249-09-0P 105280-06-6P 105280-07-7P 105280-08-8P 105280-09-9P
105280-10-2P 105280-11-3P 105280-12-4P
105280-13-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as anticoagulant)
IT **105280-10-2P 105280-11-3P 105280-13-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as anticoagulant)
RN 105280-10-2 HCAPLUS
CN Cyclohexanecarboxylic acid, 1-[[3-(1H-imidazol-1-ylmethyl)-1H-indazol-1-yl]methyl]-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



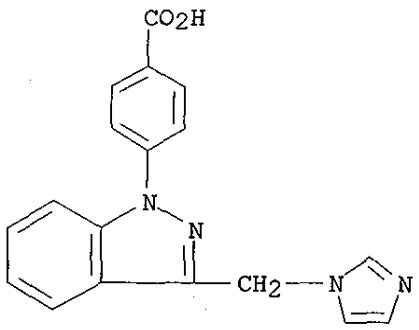
● HCl

RN 105280-11-3 HCAPLUS
CN Cyclohexanecarboxylic acid, 1-[[3-(1H-imidazol-1-ylmethyl)-1H-indazol-1-yl]methyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

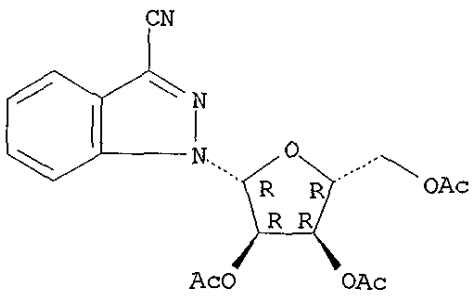
RN 105280-13-5 HCAPLUS
CN Benzoic acid, 4-[3-(1H-imidazol-1-ylmethyl)-1H-indazol-1-yl]-, sodium salt (9CI) (CA INDEX NAME)



● Na

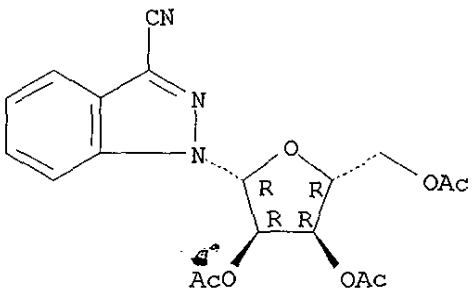
L7 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1974:463915 HCAPLUS
DOCUMENT NUMBER: 81:63915
TITLE: Glycosides of pyrazole and condensed pyrazole systems. V. 1-Glycosides of 3-substituted indazoles
AUTHOR(S): Korbukh, I. A.; Blanko, F. F.; Preobrazhenskaya, M. N.
CORPORATE SOURCE: USSR
SOURCE: Zhurnal Organicheskoi Khimii (1974), 10(5), 1091-5
CODEN: ZORKAE; ISSN: 0514-7492
DOCUMENT TYPE: Journal
LANGUAGE: Russian
GI For diagram(s), see printed CA Issue.
AB Heating 3-cyanoindazole with tetra-O-acetyl-D-ribofuranose 30 min at 170° in the presence of iodine gave 55% ribofuranoside (I; R = Ac, R1 = CN) which was hydrolyzed by NH3-MeOH to yield 90% ribofuranoside (I; R = H, R1 = CN). Oxidation of the acetate by boiling an NH3 solution containing H2O2 3 hr gave 80% amide (I; R = H, R1 = CONH2). 3-Chloroindazole treated with tetra-O-acetyl-D-ribofuranose, followed by hydrolysis gave 65% chloro derivative (I; R = H, R1 = Cl).
CC 33-8 (Carbohydrates)
Section cross-reference(s): 28
IT **42215-74-7P** 42215-75-8P 53225-56-2P 53225-57-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
IT **42215-74-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 42215-74-7 HCAPLUS
CN 1H-Indazole-3-carbonitrile, 1-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1973:405518 HCAPLUS
DOCUMENT NUMBER: 79:5518
TITLE: Synthesis of 1-β-D-ribofuranosyl-3-cyanoindazole
AUTHOR(S): Korbukh, I. A.; Blanko, F. F.; Preobrazhenskaya, M. N.
CORPORATE SOURCE: Inst. Eksp. Klin. Onkol., Moscow, USSR
SOURCE: Zhurnal Organicheskoi Khimii (1973), 9(4), 852-3
CODEN: ZORKAE; ISSN: 0514-7492
DOCUMENT TYPE: Journal
LANGUAGE: Russian
GI For diagram(s), see printed CA Issue.
AB The title compound (I) was prepared by heating 3-cyanoindazole with tetra-O-acetylribofuranose in vacuo at 170° in the presence of iodine to give I triacetae, which was deacetylated by NH3 in MeOH.
CC 33-2 (Carbohydrates)
IT **42215-74-7P** 42215-75-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
IT **42215-74-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 42215-74-7 HCAPLUS
CN 1H-Indazole-3-carbonitrile, 1-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



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